Access DB# 129646

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: _____ Examiner # :_____ Date: _____
Art Unit: _____ Phone Number 30_____ Serial Number: _____
Mail Box and Bldg/Room Location: _____ Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

_____

Earliest Priority Filing Date: _____

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

****

STAFF USE ONLY		Type of Search		Vendors and cost where applicable	
Searcher:		NA Sequence (#)		STN	✓
Searcher Phone #:	22504	AA Sequence (#)		Dialog	
Searcher Location:		Structure (#)		Questel/Orbit	
Date Searcher Picked Up:	8/12	Bibliographic	✓	Dr.Link	
Date Completed:	8/12	Litigation		Lexis/Nexis	
Searcher Prep & Review Time:		Fulltext		Sequence Systems	
Clerical Prep Time:	15	Patent Family		WWW/Internet	
Online Time:	545	Other		Other (specify)	

PTO-1590 (8-01)

STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 129646

TO: Emily M Le **Location: 3c35 / 3c18** **Thursday, August 12, 2004** **Art Unit: 1648** **Phone: 272-0903** **Serial Number: 09 / 936449**	**From: Jan Delaval** **Location: Biotech-Chem Library** **Rem 1A51** **Phone: 272-2504** **jan.delaval@uspto.gov**

Search Notes

129646

Delaval, Jan

From: Le, Emily
Sent: Wednesday, August 11, 2004 10:24 AM
To: Delaval, Jan
Subject: STN search: 09/936449

Jan,

Please provide a search for the following concept:
1. coumarin and chaperone
2. coumarin and chaperone and heat shock

synonyms:
coumarin: novobiocin, chlorobiocin, $hydroxycoumarin, dicumarol, warfarin, phenprocoumon, coumermycin
chaperone: chaperonin, heat shock protein (particularly heat schock protein 90, also known as Hsp90).

priority date: 03/12/1999

inventors: http://expoweb1:8001/cgi-bin/expo/GenInfo/sninventors.pl?APPL_ID=09936449

Thanks, Jan!

Emily Le
Remsen, 3C35
(571) 272-0903

```
=> d his

     (FILE 'HOME' ENTERED AT 09:01:18 ON 12 AUG 2004)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 09:01:33 ON 12 AUG 2004
               E COUMARIN/CN
L1           1 S E3
               E NOVOBIOCIN/CN
L2           1 S E3
               E CHLOROBIOCIN/CN
L3           1 S E3
               E HYDROXYCOUMARIN/CN
L4           1 S E3
               E DICUMAROL/CN
L5           1 S E3
               E WARFARIN/CN
L6           1 S E3
               E PHENPROCOUMON/CN
L7           1 S E3
               E COUMERMYCIN/CN
L8           1 S E3
L9           8 S L1-L8
               SEL RN
L10        213 S E1-E8/CRN
L11        130 S L10 NOT (PMS OR IDS OR MXS OR MNS)/CI
L12         21 S L11 NOT (COMPD OR WITH OR UNSPECIFIED OR CONJUGATE)
L13        192 S L10 NOT L12
L14      10774 S COUMARIN OR NOVOBIOCIN OR CHLOROBIOCIN OR HYDROXYCOUMARIN OR
L15      10680 S L14 NOT L9,L10

     FILE 'HCAPLUS' ENTERED AT 09:05:11 ON 12 AUG 2004
L16      14477 S L9 OR L12
L17        219 S L13
L18      33774 S L15
L19      42695 S ?COUMARIN? OR ?NOVOBIOCIN? OR ?CHLOROBIOCIN? OR ?HYDROXYCOUMA
L20       1187 S COUMADIN? OR 2H 1 BENZOPYRAN 2 ONE
L21       1146 S DICOUMAROL
L22      57132 S L16-L21
               E HEAT SHOCK PROTEIN/CT
L23      21562 S HEAT SHOCK(L)PROTEIN
               E HEAT-SHOCK/CT
L24       1699 S E62-E65
L25       9914 S E32-E61,E66-E68
               E E32+ALL
L26      15973 S E3-E6,E2+NT
               E HSP90
L27       2401 S E3-E19
L28          5 S E34
L29       3101 S HSP90 OR HSP 90
               E CHAPERONE/CT
               E E4+ALL
               E E2+ALL
L30       6435 S E3,E4,E2+NT
               E CHAPERONIN/CT
L31       2560 S E6-E12
               E E6+ALL
L32      11816 S CHAPERON?
L33         90 S L22 AND L23-L32
L34         51 S L33 AND (PD<=19990312 OR PRD<=19990312 OR AD<=19990312)
               E MARCU M/AU
L35         65 S E3,E4,E16,E17
               E MECKERS L/AU
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                E NECKERS L/AU
L36          220 S E3-E8
                E SCHULTE T/AU
L37           37 S E3,E7,E9-E13
L38            4 S L33 AND L35-L37
L39            1 S L34 AND L38
L40            4 S L38,L39
L41           50 S L34 NOT L40
L42            7 S L41 AND (PHARMACEUT? OR PHARMACOL?)/SC,SX
                SEL DN AN 2 5 6 7 L42
L43            4 S L42 AND E1-E12
L44           43 S L41 NOT L42
                SEL DN AN L44 5 19 30 33 36 37 43
L45            7 S L44 AND E13-E33
L46           15 S L40,L43,L45 AND L16-L45
L47           15 S L46 AND (HSP? OR HEAT SHOCK OR ?PROTEIN? OR 90)
L48            3 S L47 AND ?CHAPERON?
L49           15 S L47,L48
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 09:23:40 ON 12 AUG 2004
L50            7 S E34-E40
L51            3 S L50 AND L9,L12
L52            4 S L50 AND L13,L15
L53           12 S L9,L50-L52

=> fil reg
FILE 'REGISTRY' ENTERED AT 09:24:39 ON 12 AUG 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   11 AUG 2004  HIGHEST RN 725685-10-9
DICTIONARY FILE UPDATES:  11 AUG 2004  HIGHEST RN 725685-10-9

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d ide can tot l53

L53  ANSWER 1 OF 12  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   78040-85-4  REGISTRY
CN   Coumermycin (7CI, 9CI)  (CA INDEX NAME)
MF   Unspecified
CI   MAN
LC   STN Files:   AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS,
       EMBASE, IPA, NAPRALERT, PHAR, TOXCENTER, USPATFULL
DT.CA  CAplus document type:  Conference; Journal; Patent
RL.P   Roles from patents:  ANST (Analytical study); BIOL (Biological study);
       OCCU (Occurrence); PREP (Preparation); PROC (Process); USES (Uses)
RLD.P  Roles for non-specific derivatives from patents:  BIOL (Biological
```

study); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PROC (Process); PRP (Properties); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
69 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
69 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 141:82297

REFERENCE 2: 140:105321

REFERENCE 3: 140:88377

REFERENCE 4: 139:194893

REFERENCE 5: 136:259921

REFERENCE 6: 136:98820

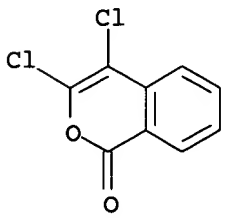
REFERENCE 7: 136:689

REFERENCE 8: 135:339201

REFERENCE 9: 135:133932

REFERENCE 10: 135:51028

L53 ANSWER 2 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN **51050-59-0** REGISTRY
CN 1H-2-Benzopyran-1-one, 3,4-dichloro- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **3,4-Dichloroisocoumarin**
FS 3D CONCORD
MF C9 H4 Cl2 O2
LC STN Files: AGRICOLA, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, MEDLINE, MSDS-OHS, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Conference; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
84 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:402221

REFERENCE 2: 140:389052

REFERENCE 3: 140:315899

REFERENCE 4: 140:175176

REFERENCE 5: 140:157485

REFERENCE 6: 140:82342

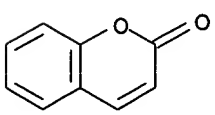
REFERENCE 7: 140:38536

REFERENCE 8: 139:318425

REFERENCE 9: 139:288166

REFERENCE 10: 139:129917

L53 ANSWER 3 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN 43070-85-5 REGISTRY
CN 2H-1-Benzopyran-2-one, hydroxy- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Coumarin, hydroxy- (7CI)
OTHER NAMES:
CN Hydroxy-2H-1-benzopyran-2-one
CN **Hydroxycoumarin**
CN Oxycoumarin
MF C9 H6 O3
CI IDS
LC STN Files: AGRICOLA, AQUIRE, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, EMBASE, NAPRALERT, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Conference; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)



D1—OH

62 REFERENCES IN FILE CA (1907 TO DATE)
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63 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 141:11954

REFERENCE 2: 140:368059

REFERENCE 3: 140:292209

REFERENCE 4: 140:154111

REFERENCE 5: 140:154092

REFERENCE 6: 140:89776

REFERENCE 7: 139:360902

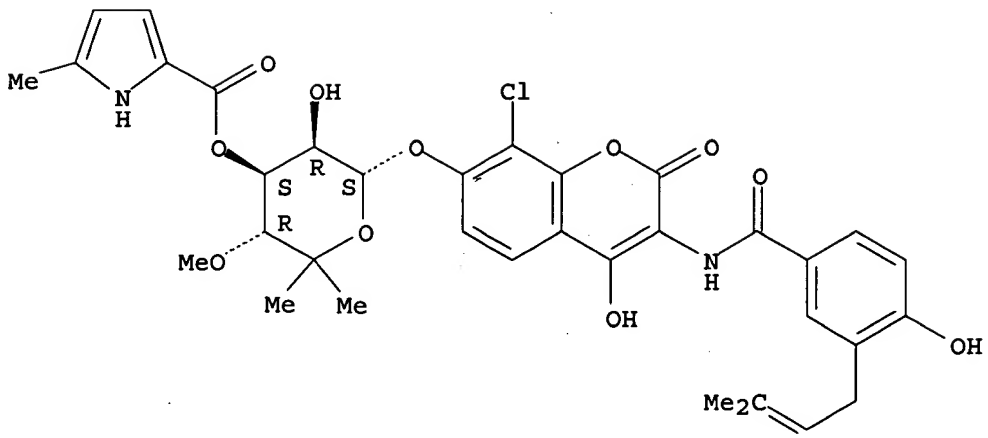
REFERENCE 8: 139:311934

REFERENCE 9: 139:280895

REFERENCE 10: 139:280893

L53 ANSWER 4 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN **39868-96-7** REGISTRY
CN Benzamide, N-[8-chloro-7-[[6-deoxy-5-C-methyl-4-O-methyl-3-O-[(5-methyl-1H-pyrrol-2-yl)carbonyl]-α-L-lyxo-hexopyranosyl]oxy]-4-hydroxy-2-oxo-2H-1-benzopyran-3-yl]-4-hydroxy-3-(3-methyl-2-butenyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Pyrrole-2-carboxylic acid, 5-methyl-, 3'-ester with N-[8-chloro-7-[(6-deoxy-5-C-methyl-4-O-methyl-α-L-lyxo-hexopyranosyl)oxy]-4-hydroxy-2-oxo-2H-1-benzopyran-3-yl]-4-hydroxy-3-(3-methyl-2-butenyl)benzamide
OTHER NAMES:
CN 18631RP
CN Antibiotic 2562A
CN **Chlorobiocin**
CN Clorobiocin
CN NSC 227186
CN RP 18631
FS STEREOSEARCH
DR 9037-72-3, 36631-40-0, 69343-32-4, 26637-98-9, 34628-96-1
MF C35 H37 Cl N2 O11
CI COM
LC STN Files: BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, RTECS*, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); PROC (Process); PRP (Properties)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

49 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
52 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:265188

REFERENCE 2: 140:159453

REFERENCE 3: 140:76987

REFERENCE 4: 140:58478

REFERENCE 5: 139:377683

REFERENCE 6: 139:303700

REFERENCE 7: 139:64106

REFERENCE 8: 139:18887

REFERENCE 9: 138:182118

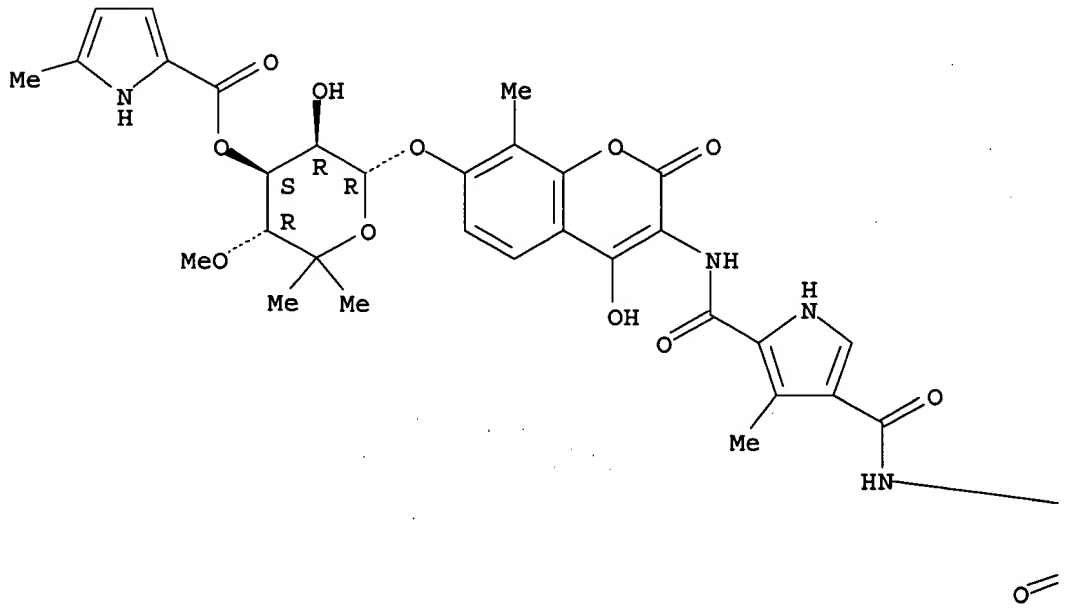
REFERENCE 10: 137:87839

L53 ANSWER 5 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN **4434-05-3** REGISTRY
CN 1H-Pyrrole-2,4-dicarboxamide, N,N'-bis[7-[[6-deoxy-5-C-methyl-4-O-methyl-3-O-[(5-methyl-1H-pyrrol-2-yl)carbonyl]-α-L-lyxo-hexopyranosyl]oxy]-4-hydroxy-8-methyl-2-oxo-2H-1-benzopyran-3-yl]-3-methyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Pyrrole-2-carboxylic acid, 5-methyl-, diester with N,N'-bis[7-[(6-deoxy-5-C-methyl-4-O-methyl-α-L-lyxo-hexopyranosyl)oxy]-4-hydroxy-8-methyl-2-oxo-2H-1-benzopyran-3-yl]-3-methyl-1H-pyrrole-2,4-dicarboxamide
CN **Coumarin, 3,3'-[(3-methylpyrrole-2,4-diyl)bis(carbonylimino)]bis[7-[(5,5-di-C-methyl-4-O-methyl-α-L-lyxopyranosyl)oxy]-4-hydroxy-8-methyl-, bis(5-methylpyrrole-2-carboxylate) (ester) (8CI)**
CN **Coumermycin A1 (7CI)**
CN **Pyrrole-2-carboxylic acid, 5-methyl-, diester with 3,3'-[(3-methylpyrrole-2,4-diyl)bis(carbonylimino)]bis[7-[(5,5-di-C-methyl-4-O-methyl-α-L-lyxopyranosyl)oxy]-4-hydroxy-8-methylcoumarin] (8CI)**

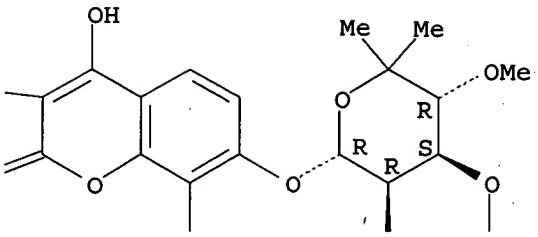
OTHER NAMES:
CN Coumamycin
CN Notomycin A1
CN NSC 107412
FS STEREOSEARCH
DR 11035-12-4, 1372-92-5, 22260-48-6, 22850-02-8, 23249-07-2, 30418-37-2, 30546-09-9
MF C55 H59 N5 O20
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSDRUGNEWS, IMSRESEARCH, IPA, MEDLINE, MSDS-OHS, PHAR, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties)

Absolute stereochemistry.

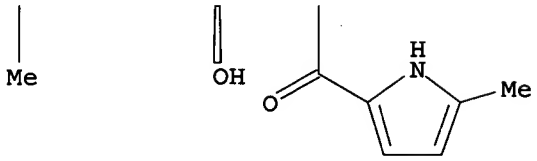
PAGE 1-A



PAGE 1-B



PAGE 2-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

202 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
202 REFERENCES IN FILE CAPLUS (1907 TO DATE)
7 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 140:265188

REFERENCE 2: 140:123415

REFERENCE 3: 139:242267

REFERENCE 4: 139:240318

REFERENCE 5: 139:97752

REFERENCE 6: 139:64106

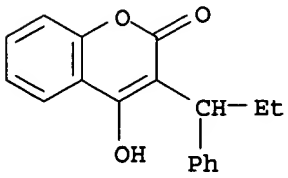
REFERENCE 7: 138:354143

REFERENCE 8: 138:332654

REFERENCE 9: 138:270349

REFERENCE 10: 138:182118

L53 ANSWER 6 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN 435-97-2 REGISTRY
CN 2H-1-Benzopyran-2-one, 4-hydroxy-3-(1-phenylpropyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Coumarin, 3-(α-ethylbenzyl)-4-hydroxy- (8CI)
OTHER NAMES:
CN (±)-Phenprocoumon
CN 3-(α-Ethylbenzyl)-4-hydroxycoumarin
CN 3-(α-Phenylpropyl)-4-hydroxycoumarin
CN 3-(1-Phenylpropyl)-4-hydroxycoumarin
CN 4-Hydroxy-2-oxo-3-(1-phenylpropyl)-2H-chromene
CN DL-3-(α-Ethylbenzyl)-4-hydroxycoumarin
CN Falithrom
CN Fencumar
CN Liquamar
CN Marcoumar
CN Marcumar
CN Phenprocoumarol
CN Phenprocoumarole
CN **Phenprocoumon**
CN Ro 1-4849
FS 3D CONCORD
DR 5999-41-7
MF C18 H16 O3
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PS, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses); NORL (No role in record)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

448 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
449 REFERENCES IN FILE CAPLUS (1907 TO DATE)
8 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 141:64421

REFERENCE 2: 141:17265

REFERENCE 3: 141:16830

REFERENCE 4: 141:16692

REFERENCE 5: 140:228933

REFERENCE 6: 140:191764

REFERENCE 7: 140:174382

REFERENCE 8: 140:174256

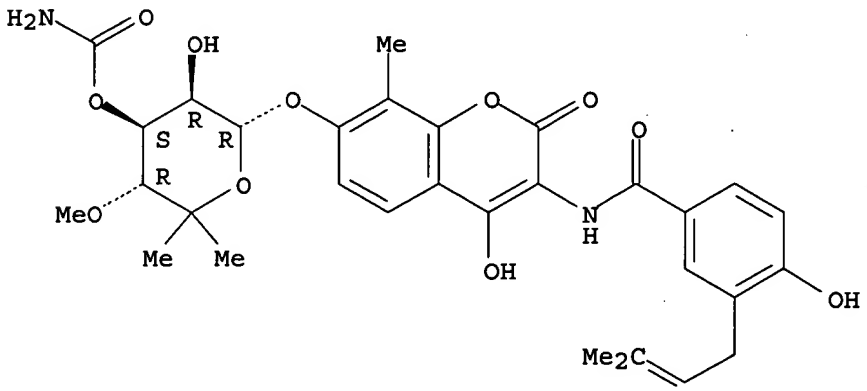
REFERENCE 9: 140:139020

REFERENCE 10: 140:12770

L53 ANSWER 7 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN **303-81-1** REGISTRY
CN Benzamide, N-[7-[[3-O-(aminocarbonyl)-6-deoxy-5-C-methyl-4-O-methyl-α-L-lyxo-hexopyranosyl]oxy]-4-hydroxy-8-methyl-2-oxo-2H-1-benzopyran-3-yl]-4-hydroxy-3-(3-methyl-2-butenyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Coumarin, 7-[4-(carbamoyloxy)tetrahydro-3-hydroxy-5-methoxy-6,6-dimethylpyran-2-yloxy]-4-hydroxy-3-[4-hydroxy-3-(3-methyl-2-butenyl)benzamido]-8-methyl- (6CI)
CN **Novobiocin (8CI)**
OTHER NAMES:
CN Albamix
CN Albamycin
CN Antibiotic PA-93
CN Cardelmycin
CN Cathocin
CN Cathomycin
CN Crystallinic acid
CN Inamycin
CN Novo-R
CN PA 93
CN Robiocina
CN Sirbiocina
CN Spheromycin
CN Stilbiocina
CN Streptonivicin
CN U 6391
FS STEREOSEARCH
DR 8028-29-3, 107781-69-1
MF C31 H36 N2 O11
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PROMT, PS, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study);

PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1915 REFERENCES IN FILE CA (1907 TO DATE)
11 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1923 REFERENCES IN FILE CAPLUS (1907 TO DATE)
80 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 141:111566

REFERENCE 2: 141:88025

REFERENCE 3: 141:82294

REFERENCE 4: 141:68099

REFERENCE 5: 141:20357

REFERENCE 6: 141:4024

REFERENCE 7: 141:4020

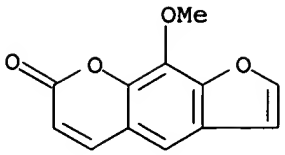
REFERENCE 8: 141:3658

REFERENCE 9: 140:420526

REFERENCE 10: 140:388532

L53 ANSWER 8 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN **298-81-7** REGISTRY
CN 7H-Furo[3,2-g][1]benzopyran-7-one, 9-methoxy- (8CI, 9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:

CN 5-Benzofuranacrylic acid, 6-hydroxy-7-methoxy-, δ-lactone (7CI)
OTHER NAMES:
CN **8-Methoxy-6,7-furanocoumarin**
CN 8-Methoxypsoralen
CN 8-Methoxypsoralene
CN 8-Methoxy[furano-3',2':6,7-coumarin]
CN 8-MOP
CN 8-MP
CN Ammodin
CN Ammoidin
CN Deltapsoralen
CN Geroxalen
CN Meladinin
CN Meladinine
CN Meladoxen
CN Meloxine
CN Methoxa-Dome
CN Methoxsalen
CN New-Meladinin
CN NSC 45923
CN Oxsoralen
CN Oxsoralen Lotion
CN Oxsoralen-Ultra
CN Oxypsoralen
CN Puvalen
CN Puvamet
CN Uvadex
CN Xanthotoxin
CN Xanthotoxine
FS 3D CONCORD
DR 12692-94-3
MF C12 H8 O4
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PIRA, PROMT, PS, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2979 REFERENCES IN FILE CA (1907 TO DATE)
99 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2984 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 141:105262

REFERENCE 2: 141:98979

REFERENCE 3: 141:84016

REFERENCE 4: 141:68239

REFERENCE 5: 141:66689

REFERENCE 6: 141:49976

REFERENCE 7: 141:49677

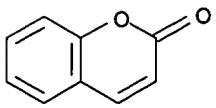
REFERENCE 8: 141:36293

REFERENCE 9: 141:35573

REFERENCE 10: 141:35559

L53 ANSWER 9 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN **91-64-5** REGISTRY
CN 2H-1-Benzopyran-2-one (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Coumarin (8CI)**
OTHER NAMES:
CN 1,2-Benzopyrone
CN 2-Propenoic acid, 3-(2-hydroxyphenyl)-, δ-lactone
CN 5,6-Benzo-2-pyrone
CN Benzo-α-pyrone
CN cis-o-Coumarinic acid lactone
CN Coumarinic anhydride
CN NSC 8774
CN o-Hydroxycinnamic acid lactone
CN Rattex
CN Tonka bean camphor
FS 3D CONCORD
MF C9 H6 O2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL

(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7095 REFERENCES IN FILE CA (1907 TO DATE)
1536 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
7108 REFERENCES IN FILE CAPLUS (1907 TO DATE)
10 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 141:103353

REFERENCE 2: 141:103129

REFERENCE 3: 141:98979

REFERENCE 4: 141:94452

REFERENCE 5: 141:94403

REFERENCE 6: 141:93467

REFERENCE 7: 141:90917

REFERENCE 8: 141:88915

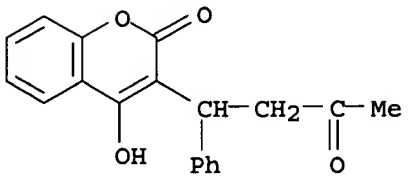
REFERENCE 9: 141:81675

REFERENCE 10: 141:73658

L53 ANSWER 10 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN 81-81-2 REGISTRY
CN 2H-1-Benzopyran-2-one, 4-hydroxy-3-(3-oxo-1-phenylbutyl)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:
CN Coumarin, 3-(α-acetonylbenzyl)-4-hydroxy- (7CI, 8CI)
OTHER NAMES:
CN (±)-Warfarin
CN (±)-Warfarin-alcohol
CN (RS)-Warfarin
CN 1-(4'-Hydroxy-3'-coumarinyl)-1-phenyl-3-butanone
CN 3-(α-Acetonylbenzyl)-4-hydroxycoumarin
CN 3-(α-Phenyl-β-acetylethyl)-4-hydroxycoumarin
CN 3-(1'-Phenyl-2'-acetylethyl)-4-hydroxycoumarin
CN 4-Hydroxy-3-(3-oxo-1-phenylbutyl)-2H-chromen-2-one
CN Athrombine-K
CN Brumolin
CN Co-Rax
CN Compound 42
CN Coumafen
CN Coumafene
CN Coumaphen
CN Coumefene
CN Dethmor
CN DL-3-(α-Acetonylbenzyl)-4-hydroxycoumarin
CN Kumader
CN Kumadu
CN Kumatox
CN NSC 59813
CN rac-Warfarin
CN Ratron
CN Ratron G
CN Rodafarin
CN Rodafarin C
CN Rodex
CN Temus W
CN Vampirinip II
CN Vampirinip III
CN W.A.R.F. 42
CN WARF compound 42
CN **Warfarin**
CN Zoocoumarin
FS 3D CONCORD
DR 56573-89-8, 5543-56-6
MF C19 H16 O4
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DIOGENES, EMBASE, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PIRA, PROMT, PS, RTECS*, SPECINFO, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical

study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3455 REFERENCES IN FILE CA (1907 TO DATE)
49 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3466 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 141:101526

REFERENCE 2: 141:99392

REFERENCE 3: 141:94452

REFERENCE 4: 141:81658

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REFERENCE 6: 141:81562

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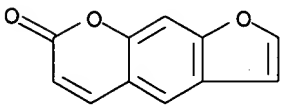
REFERENCE 8: 141:76895

REFERENCE 9: 141:69470

REFERENCE 10: 141:64757

L53 ANSWER 11 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN **66-97-7** REGISTRY
CN 7H-Furo[3,2-g][1]benzopyran-7-one (8CI, 9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Furocoumarin (6CI)**
OTHER NAMES:
CN 2-Propenoic acid, 3-(6-hydroxy-5-benzofuranyl)-, δ-lactone
CN **6,7-Furanocoumarin**
CN Ficusin
CN **Furo[2',3':7,6]coumarin**
CN **Furo[4',5':6,7]coumarin**
CN NSC 404562
CN Psoralen
CN Psoralene
FS 3D CONCORD
MF C11 H6 O3
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HSDB*, IFICDB,

IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PROMT, RTECS*, SPECINFO, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2034 REFERENCES IN FILE CA (1907 TO DATE)
598 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2036 REFERENCES IN FILE CAPLUS (1907 TO DATE)
31 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 141:105262

REFERENCE 2: 141:85492

REFERENCE 3: 141:84727

REFERENCE 4: 141:50444

REFERENCE 5: 141:49162

REFERENCE 6: 141:36293

REFERENCE 7: 141:22217

REFERENCE 8: 141:19881

REFERENCE 9: 141:18849

REFERENCE 10: 141:18689

L53 ANSWER 12 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN 66-76-2 REGISTRY
CN 2H-1-Benzopyran-2-one, 3,3'-methylenebis[4-hydroxy- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Coumarin, 3,3'-methylenebis[4-hydroxy- (8CI)
OTHER NAMES:

CN 3,3'-Methylenebis[4-hydroxy-1,2-benzopyrone]
CN 3,3'-Methylenebis[4-hydroxycoumarin]
CN Acadyl
CN Acavyl
CN Antitrombosin
CN Baracoumin
CN Bis(4-hydroxycoumarin-3-yl)methane
CN Bis-3,3'-(4-hydroxycoumarinyl)methane
CN Bishydroxycoumarin
CN Cuma
CN Cumid
CN Di-4-hydroxy-3,3'-methylenedicoumarin
CN Dicoumal
CN Dicoumarin
CN Dicoumarol
CN Dicuman
CN Dicumarine
CN **Dicumarol**
CN Dicumol
CN Dufalone
CN Kumoran
CN Melitoxin
CN NC 034
CN NSC 17860
CN NSC 221570
CN NSC 41834
CN Temparin
CN Trombosan
FS 3D CONCORD
MF C19 H12 O6
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, HODOC*, HSDB*, IFICDB, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
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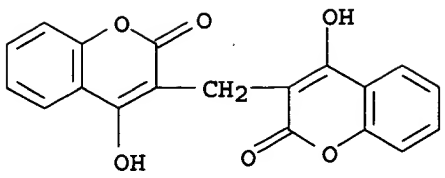

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1552 REFERENCES IN FILE CA (1907 TO DATE)
20 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1553 REFERENCES IN FILE CAPLUS (1907 TO DATE)
26 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 141:33315

REFERENCE 2: 141:2997

REFERENCE 3: 140:394622

REFERENCE 4: 140:316401

REFERENCE 5: 140:297538

REFERENCE 6: 140:228342

REFERENCE 7: 140:169447

REFERENCE 8: 140:169387

REFERENCE 9: 140:90438

REFERENCE 10: 140:87232

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 09:24:50 ON 12 AUG 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 12 Aug 2004 VOL 141 ISS 7
FILE LAST UPDATED: 11 Aug 2004 (20040811/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr tot l49

L49 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:302095 HCAPLUS
DN 139:159280
ED Entered STN: 20 Apr 2003
TI Development of small molecule **Hsp90** inhibitors: Utilizing both forward and reverse chemical genomics for drug identification
AU **Neckers, Len**
CS Cell and Cancer Biology Branch, National Cancer Institute, NIH, Rockville, MD, 20850, USA
SO Current Medicinal Chemistry (2003), 10(9), 733-739
CODEN: CMCHE7; ISSN: 0929-8673
PB Bentham Science Publishers Ltd.
DT Journal; General Review
LA English
CC 1-0 (Pharmacology)
AB A review. **Heat shock protein 90** (**Hsp90**) is a mol. **chaperone** whose association is required for stability and function of multiple mutated, chimeric, and over-expressed signaling **proteins** that promote cancer cell growth and/or survival. **Hsp90** client **proteins** include mutated p53, Bcr-Abl, Raf-1, Akt, HER2/Neu (ErbB2), and HIF-1α. **Hsp90** inhibitors, by interacting specifically with a single mol. target, cause the destabilization and eventual degradation of **Hsp90** client **proteins**, and they have also shown promising antitumor activity in preclin. model systems. One **Hsp90** inhibitor, 17-AAG, is currently in Phase 1 clin. trial. **Hsp90** inhibitors are unique in that, although they are directed towards a specific mol. target, they simultaneously inhibit multiple signaling pathways on which cancer cells depend for growth and survival. Benzoquinone ansamycin binding to **Hsp90** led to the identification of radicicol as an addnl. **Hsp90** inhibitor. Addnl. target-based screening uncovered **novobiocin** as a third structurally distinct small mol. with **Hsp90** inhibitory properties. Use of **novobiocin**, in turn, led to identification of a previously uncharacterized C-terminal ATP binding site in the **chaperone**. Small mol. inhibitors of **Hsp90** have been very useful in understanding **Hsp90** biol. and in validating this **protein** as a mol. target for anti-cancer drug development.
ST review antitumor **Hsp90** inhibitor design genomics
IT **Heat-shock proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**HSP 90**; development of **Hsp90** inhibitors)
IT Antitumor agents
Drug design
Neoplasm
(development of **Hsp90** inhibitors)
RE.CNT 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Aligue, R; Embo J 1994, V13, P6099 HCAPLUS
(2) An, W; Cell Growth Differ 2000, V11, P355 HCAPLUS
(3) Bagatell, R; Clin Cancer Res 2001, V7, P2076 HCAPLUS
(4) Basso, A; J Biol Chem 2002, V277, P39858 HCAPLUS
(5) Basso, A; Oncogene 2002, V21, P1159 HCAPLUS
(6) Bilwes, A; Cell 1999, V96, P131 HCAPLUS
(7) Blagosklonny, M; Proc Natl Acad Sci USA 1996, V93, P8379 HCAPLUS
(8) Bonvini, P; Cancer Res 2002, V62, P1559 HCAPLUS
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(11) Chavany, C; J Biol Chem 1996, V271, P4974 HCAPLUS
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(16) Ferrarini, M; Int J Cancer 1992, V51, P613 HCAPLUS
(17) Garnier, C; J Biol Chem 2002, V277, P12208 HCAPLUS
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L49 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:871655 HCAPLUS
DN 134:159112

ED Entered STN: 13 Dec 2000
TI The **heat shock protein 90** antagonist **novobiocin** interacts with a previously unrecognized ATP-binding domain in the carboxyl terminus of the **chaperone**
AU **Marcu, Monica G.**; Chadli, Ahmed; Bouhouche, Ilham; Catelli, Maria; **Neckers, Leonard M.**
CS Department of Cell and Cancer Biology, Medicine Branch, NCI, National Institutes of Health, Rockville, MD, 20850, USA
SO Journal of Biological Chemistry (2000), 275(47), 37181-37186
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 6-3 (General Biochemistry)
AB **Heat shock protein 90** (**Hsp90**), one of the most abundant **chaperones** in eukaryotes, participates in folding and stabilization of signal-transducing mols. including steroid hormone receptors and **protein** kinases. The amino terminus of **Hsp90** contains a non-conventional nucleotide-binding site, related to the ATP-binding motif of bacterial DNA gyrase. The anti-tumor agents geldanamycin and radicicol bind specifically at this site and induce destabilization of **Hsp90** -dependent client **proteins.** We recently demonstrated that the gyrase inhibitor **novobiocin** also interacts with **Hsp90**, altering the affinity of the **chaperone** for geldanamycin and radicicol and causing in vitro and in vivo depletion of key regulatory **Hsp90**-dependent kinases including v-Src, Raf-1, and p185ErbB2. In the present study we used deletion/mutation anal. to identify the site of interaction of **novobiocin** with **Hsp90**, and we demonstrate that the **novobiocin**-binding site resides in the carboxyl terminus of the **chaperone.** Surprisingly, this motif also recognizes ATP, and ATP and **novobiocin** efficiently compete with each other for binding to this region of **Hsp90.** **Novobiocin** interferes with association of the co-**chaperones** Hsc70 and p23 with **Hsp90.** These results identify a second site on **Hsp90** where the binding of small mol. inhibitors can significantly impact the function of this **chaperone**, and they support the hypothesis that both amino- and carboxyl-terminal domains of **Hsp90** interact to modulate **chaperone** activity.
ST **heat shock protein Hsp90** **novobiocin** ATP binding site **chaperone**
IT **Protein** motifs
(ATP and **novobiocin**-binding site; **heat shock protein 90** antagonist **novobiocin** interacts with a previously unrecognized ATP-binding domain in carboxyl terminus of **chaperone**)
IT **Heat-shock proteins**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(**HSP 90**, recombinant, full-length and deletion mutants; **heat shock protein 90** antagonist **novobiocin** interacts with a previously unrecognized ATP-binding domain in carboxyl terminus of **chaperone**)
IT Molecular association
(**heat shock protein 90** antagonist **novobiocin** interacts with a previously unrecognized ATP-binding domain in carboxyl terminus of **chaperone**)
IT **Phosphoproteins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(hsc 70 (**heat-shock** cognate, 70,000-mol.-weight);

novobiocin interferes with association of the co-**chaperones** Hsc70 and p23 with **Hsp90**)

IT **Proteins**, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(p23; **novobiocin** interferes with association of the co-**chaperones** Hsc70 and p23 with **Hsp90**)

IT **303-81-1**, **Novobiocin**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**heat shock protein 90** antagonist **novobiocin** interacts with a previously unrecognized ATP-binding domain in carboxyl terminus of **chaperone**)

IT 56-65-5, ATP, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**heat shock protein 90**-ATP interaction)

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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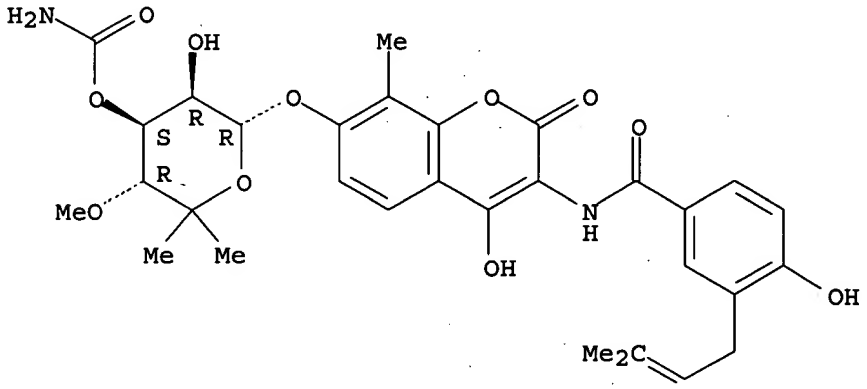
IT **303-81-1**, **Novobiocin**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**heat shock protein 90**

antagonist **novobiocin** interacts with a previously unrecognized ATP-binding domain in carboxyl terminus of **chaperone**)
RN 303-81-1 HCAPLUS
CN Benzamide, N-[7-[[3-O-(aminocarbonyl)-6-deoxy-5-C-methyl-4-O-methyl-α-L-lyxo-hexopyranosyl]oxy]-4-hydroxy-8-methyl-2-oxo-2H-1-benzopyran-3-yl]-4-hydroxy-3-(3-methyl-2-butenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L49 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:645839 HCAPLUS
DN 133:203025
ED Entered STN: 15 Sep 2000
TI Method using **coumarin** or a **coumarin** derivative for inhibiting a **chaperone protein** binding to a client **protein**
IN **Marcu, Monica G.; Neckers, Leonard M.; Schulte, Theodor W.**
PA United States Dept. of Health and Human Services, USA
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-00
CC 1-12 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000053169	A2	20000914	WO 2000-US6482	20000310 <--
	WO 2000053169	C1	20010111		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1161231	A2	20011212	EP 2000-916277	20000310 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2003523313	T2	20030805	JP 2000-603658	20000310 <--
PRAI	US 1999-124135P	P	19990312 <--		
	WO 2000-US6482	W	20000310		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2000053169	ICM	A61K031-00

AB A method is provided for inhibiting binding of a **chaperone protein** with its client **protein** or client polypeptide. The method comprises contacting **coumarin** or a **coumarin** derivative with a **chaperone protein**, such that the **coumarin** or the **coumarin** derivative binds the **chaperone protein**, which inhibits the **chaperone protein** from binding its client **protein** or client polypeptide.

ST **chaperone protein** binding inhibition **coumarin** deriv

IT **Heat-shock proteins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**HSP 90**; **coumarin** or **coumarin** derivative for inhibiting binding of **chaperone protein** to client **protein**)

IT **Proteins**, general, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(client, **chaperone protein** binding to; **coumarin** or **coumarin** derivative for inhibiting binding of **chaperone protein** to client **protein**)

IT Molecular association
Mononuclear cell (leukocyte)
Protein degradation
(**coumarin** or **coumarin** derivative for inhibiting binding of **chaperone protein** to client **protein**)

IT **Chaperonins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**coumarin** or **coumarin** derivative for inhibiting binding of **chaperone protein** to client **protein**)

IT Antibiotics
(**coumarin**; **coumarin** or **coumarin** derivative for inhibiting binding of **chaperone protein** to client **protein**)

IT Mutation
(mutated p53 **protein**; **coumarin** or **coumarin** derivative for inhibiting binding of **chaperone protein** to client **protein**)

IT p53 (**protein**)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mutated; **coumarin** or **coumarin** derivative for inhibiting binding of **chaperone protein** to client **protein**)

IT **Phospholipoproteins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pp60v-src; **coumarin** or **coumarin** derivative for inhibiting binding of **chaperone protein** to client **protein**)

IT Spleen
(splenocyte; **coumarin** or **coumarin** derivative for inhibiting binding of **chaperone protein** to client **protein**)

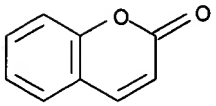
IT **91-64-5**, **Coumarin 91-64-5D**, **Coumarin**, derivs. **303-81-1**, **Novobiocin 4434-05-3**, **Coumermycin A1 39868-96-7**, **Chlorobiocin**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**coumarin** or **coumarin** derivative for inhibiting binding of **chaperone protein** to client **protein**)

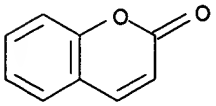
IT 9026-43-1, Serine/threonine kinase 80449-02-1, Tyrosine kinase 137632-09-8 139691-76-2, RAF-1 serine/threonine kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**coumarin** or **coumarin** derivative for inhibiting binding of **chaperone protein** to client **protein**)

IT **91-64-5, Coumarin 91-64-5D, Coumarin**, derivs. **303-81-1, Novobiocin 4434-05-3, Coumermycin** A1 **39868-96-7, Chlorobiocin**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**coumarin** or **coumarin** derivative for inhibiting binding of **chaperone protein** to client **protein**)

RN 91-64-5 HCAPLUS
CN 2H-1-Benzopyran-2-one (9CI) (CA INDEX NAME)

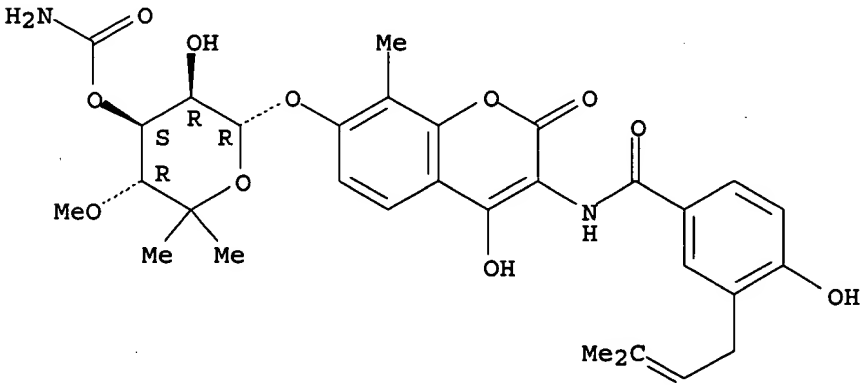


RN 91-64-5 HCAPLUS
CN 2H-1-Benzopyran-2-one (9CI) (CA INDEX NAME)



RN 303-81-1 HCAPLUS
CN Benzamide, N-[7-[[3-O-(aminocarbonyl)-6-deoxy-5-C-methyl-4-O-methyl-α-L-lyxo-hexopyranosyl]oxy]-4-hydroxy-8-methyl-2-oxo-2H-1-benzopyran-3-yl]-4-hydroxy-3-(3-methyl-2-butenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

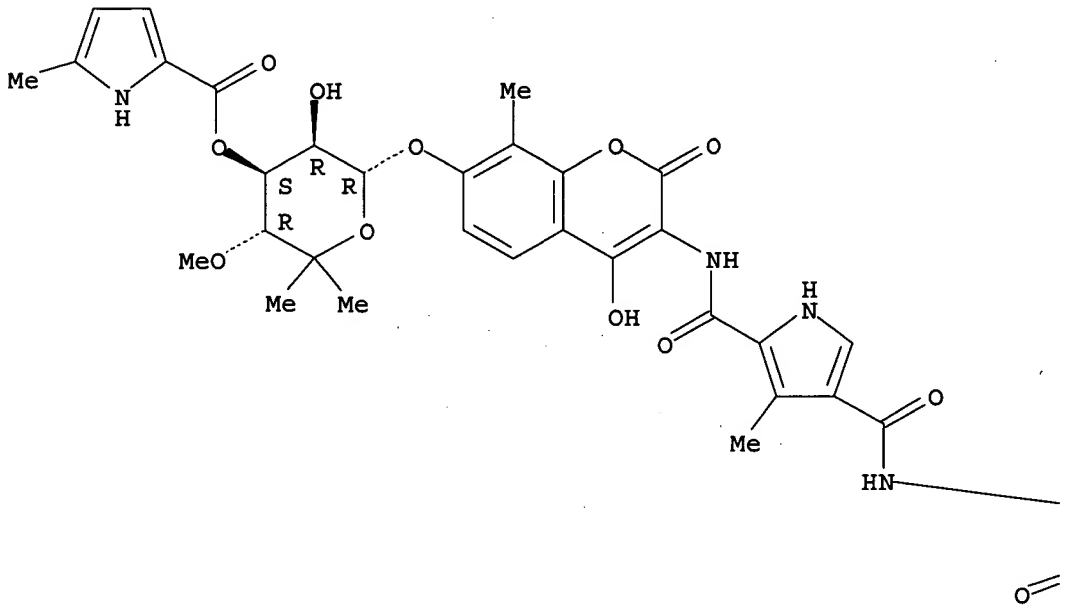


RN 4434-05-3 HCAPLUS

CN 1H-Pyrrole-2,4-dicarboxamide, N,N'-bis[7-[[6-deoxy-5-C-methyl-4-O-methyl-3-O-[(5-methyl-1H-pyrrol-2-yl)carbonyl]-α-L-lyxo-hexopyranosyl]oxy]-4-hydroxy-8-methyl-2-oxo-2H-1-benzopyran-3-yl]-3-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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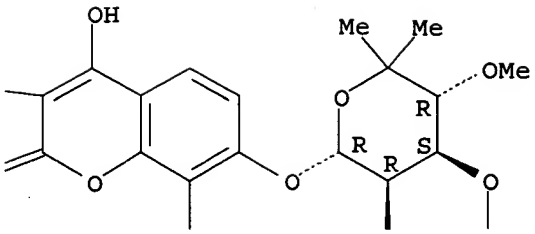

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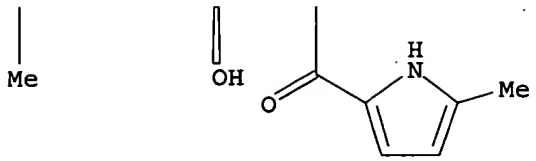
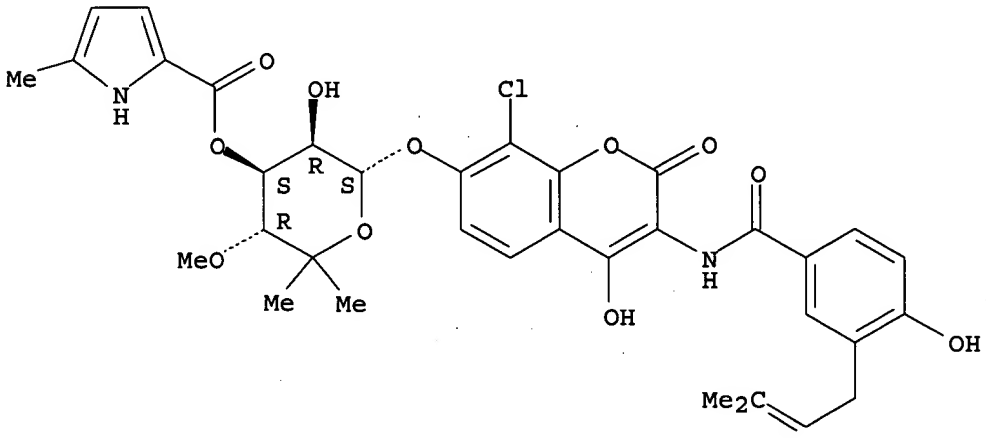


RN 39868-96-7 HCAPLUS
CN Benzamide, N-[8-chloro-7-[[6-deoxy-5-C-methyl-4-O-methyl-3-O-[(5-methyl-1H-pyrrol-2-yl)carbonyl]-α-L-lyxo-hexopyranosyl]oxy]-4-hydroxy-2-oxo-2H-1-benzopyran-3-yl]-4-hydroxy-3-(3-methyl-2-butenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L49 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:110237 HCAPLUS
DN 133:37820
ED Entered STN: 16 Feb 2000
TI **Novobiocin** and related **coumarins** and depletion of **heat shock protein 90**-dependent signaling **proteins**
AU **Marcu, Monica G.; Schulte, Theodore W.; Neckers, Leonard**
CS Department of Cell and Cancer Biology, Medicine Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD, 20850, USA
SO Journal of the National Cancer Institute (2000), 92(3), 242-248
CODEN: JNCIEQ; ISSN: 0027-8874
PB Oxford University Press
DT Journal
LA English
CC 1-6 (Pharmacology)
AB **Heat shock protein 90** (**Hsp90**) interacts with and stabilizes several oncogenic **protein** kinases (e.g., p185erbB2, p60v-src, and Raf-1) and is required for the stability and dominant-neg. function of mutated p53 **protein.** Two unrelated antibiotics, geldanamycin and radicicol, bind specifically to an atypical nucleotide-binding pocket of **Hsp90**, a site that shares homol. with the ATP-binding domain of bacterial DNA gyrase B. This interaction leads to destabilization of **proteins** that interact with **Hsp90.** Since the nucleotide-binding site of gyrase B is targeted by **coumarin**

antibiotics (e.g., **novobiocin**), we investigated whether these drugs can also interact with **Hsp90** and affect its activity. We used immobilized **novobiocin**, geldanamycin, or radicicol to isolate either endogenous **Hsp90** from cell lysates or **Hsp90** deletion fragments translated in vitro. Effects of the **coumarin** antibiotics **novobiocin**, **chlorobiocin**, and **coumermycin** A1 on several **proteins** interacting with **Hsp90** were assessed in vitro and in vivo. **Hsp90** binding to immobilized **novobiocin** was competed by soluble **coumarins** and ATP but not by geldanamycin or radicicol. A carboxy-terminal **Hsp90** fragment bound immobilized **novobiocin** but not immobilized geldanamycin, while a geldanamycin-binding amino-terminal fragment did not bind **novobiocin**. All three **coumarins** markedly reduced cellular levels of p185erbB2, p60v-src, Raf-1, and mutated p53. Furthermore, **novobiocin** reduced Raf-1 levels in the spleens of mice treated with the drug. These **coumarin** antibiotics, particularly **novobiocin**, represent a first-generation alternative to other **Hsp90**-targeting drugs that are not as well tolerated. **Novobiocin**'s unique interaction with **Hsp90** identifies an addnl. site on this **protein** amenable to pharmacol. interference with small mols.

ST **novobiocin coumarin** antibiotic **Hsp90** signaling **protein** antitumor

IT **Heat-shock proteins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**HSP 90**; **novobiocin** and related **coumarins** and depletion of **Hsp90**-dependent signaling **proteins**)

IT Drug targeting
(**Hsp90**; **novobiocin** and related **coumarins** and depletion of **Hsp90**-dependent signaling **proteins**)

IT Antibiotics
(**coumarin**; **novobiocin** and related **coumarins** and depletion of **Hsp90**-dependent signaling **proteins**)

IT Antitumor agents
Spleen
(**novobiocin** and related **coumarins** and depletion of **Hsp90**-dependent signaling **proteins**)

IT neu (receptor)
p53 (**protein**)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**novobiocin** and related **coumarins** and depletion of **Hsp90**-dependent signaling **proteins**)

IT **Phospholipoproteins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pp60v-src; **novobiocin** and related **coumarins** and depletion of **Hsp90**-dependent signaling **proteins**)

IT **Proteins**, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(signaling; **novobiocin** and related **coumarins** and depletion of **Hsp90**-dependent signaling **proteins**)

IT 142805-56-9, Topoisomerase II
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **novobiocin** and related **coumarins** and depletion of **Hsp90**-dependent signaling **proteins**)

IT 12772-57-5, Radicicol 30562-34-6, Geldanamycin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**novobiocin** and related **coumarins** and depletion of **Hsp90**-dependent signaling **proteins**)

IT **303-81-1**, **Novobiocin 4434-05-3**, **Coumermycin** A1 23214-92-8, Doxorubicin 33419-42-0, Etoposide **39868-96-7**, **Chlorobiocin**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**novobiocin** and related **coumarins** and depletion of **Hsp90**-dependent signaling **proteins**)

IT 139691-76-2
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**novobiocin** and related **coumarins** and depletion of **Hsp90**-dependent signaling **proteins**)

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD

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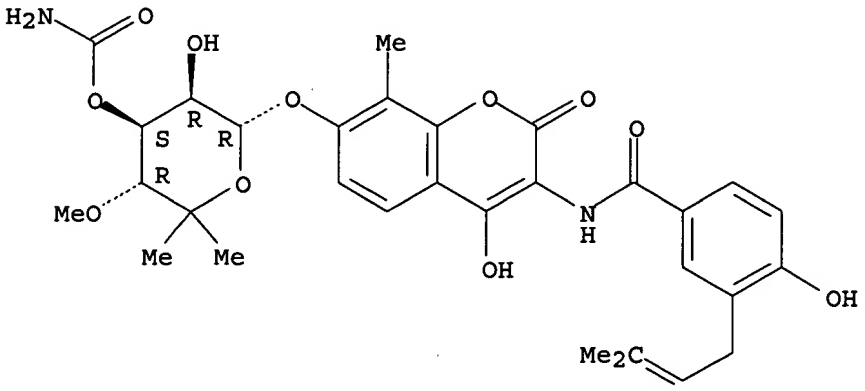
IT **303-81-1**, **Novobiocin 4434-05-3**, **Coumermycin** A1 **39868-96-7**, **Chlorobiocin**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**novobiocin** and related **coumarins** and depletion of **Hsp90**-dependent signaling **proteins**)

RN 303-81-1 HCAPLUS
CN Benzamide, N-[7-[[3-O-(aminocarbonyl)-6-deoxy-5-C-methyl-4-O-methyl-

α-L-lyxo-hexopyranosyl]oxy]-4-hydroxy-8-methyl-2-oxo-2H-1-benzopyran-3-yl]-4-hydroxy-3-(3-methyl-2-butenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

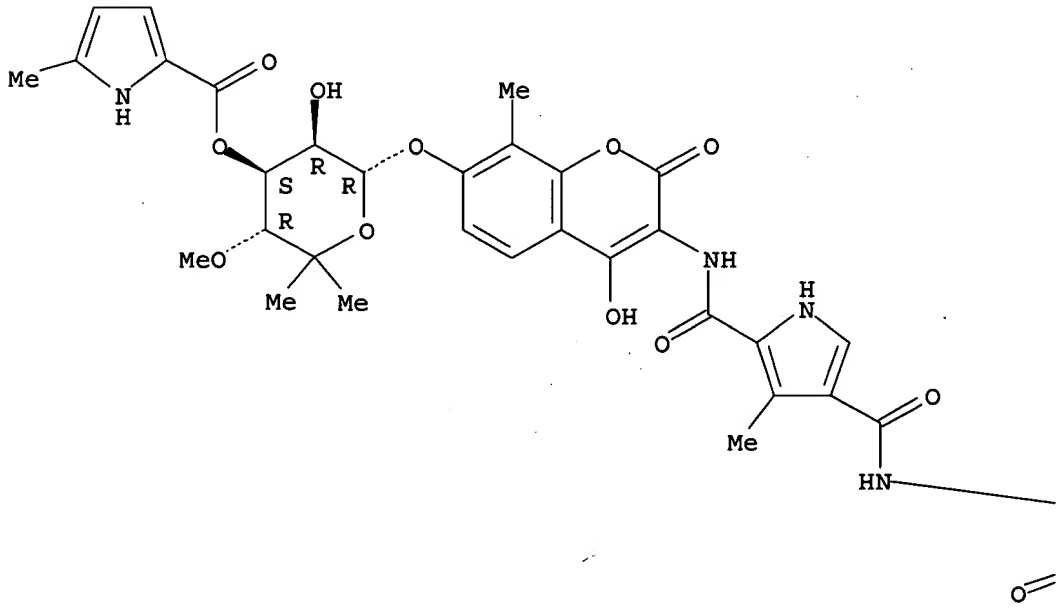


RN 4434-05-3 HCAPLUS

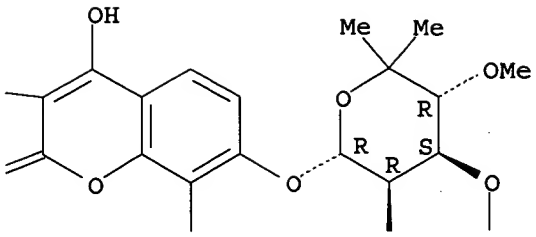
CN 1H-Pyrrole-2,4-dicarboxamide, N,N'-bis[7-[[6-deoxy-5-C-methyl-4-O-methyl-3-O-[(5-methyl-1H-pyrrol-2-yl)carbonyl]-α-L-lyxo-hexopyranosyl]oxy]-4-hydroxy-8-methyl-2-oxo-2H-1-benzopyran-3-yl]-3-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

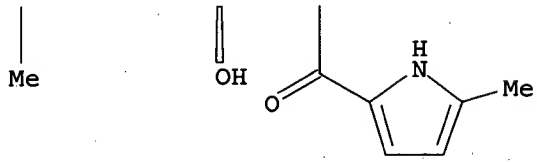
PAGE 1-A



PAGE 1-B

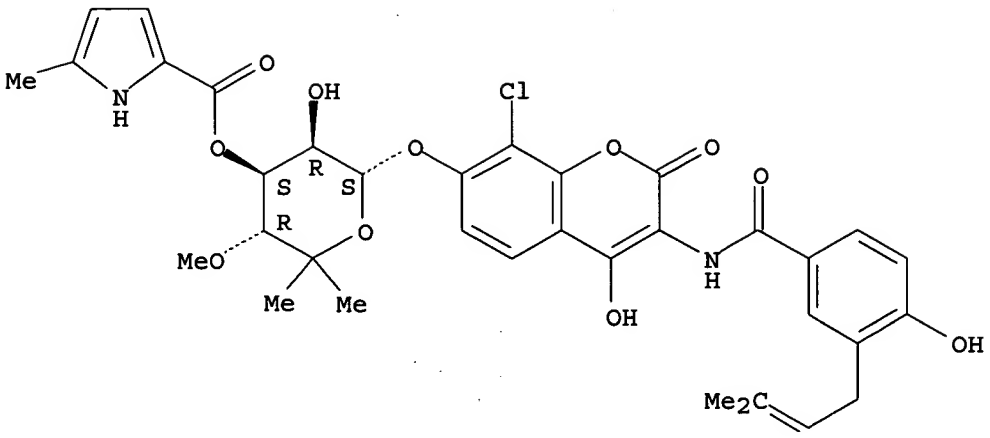


PAGE 2-B



RN 39868-96-7 HCAPLUS
CN Benzamide, N-[8-chloro-7-[[6-deoxy-5-C-methyl-4-O-methyl-3-O-[(5-methyl-1H-pyrrol-2-yl)carbonyl]-α-L-lyxo-hexopyranosyl]oxy]-4-hydroxy-2-oxo-2H-1-benzopyran-3-yl]-4-hydroxy-3-(3-methyl-2-butenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L49 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1999:48608** HCAPLUS
DN **130:119583**
ED Entered STN: 25 Jan 1999
TI Inhibitors of the NF-κB factor as activators of HSF and inducers of **heat shock proteins** for antiproliferative and antiviral therapy
IN Santoro, Maria Gabriella; Rossi, Antonio; Elia, Giuliano
PA Consiglio Nazionale Delle Ricerche, Italy
SO PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-00
CC 1-5 (**Pharmacology**)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9901117	A2	19990114	WO 1998-EP4066	19980701 <--
	WO 9901117	A3	19990401		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9888545	A1	19990125	AU 1998-88545	19980701 <--
	EP 1003492	A2	20000531	EP 1998-940106	19980701 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002507981	T2	20020312	JP 1999-506339	19980701 <--
PRAI	IT 1997-RM392	A	19970701 <--		
	WO 1998-EP4066	W	19980701 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9901117	ICM	A61K031-00

AB Inhibitors of the NF-kB factor and corresponding pharmaceutically acceptable derivative compds. to be used as activators of the HSF factor for the transcription and translation of **heat shock** genes, with production of **hsp70**, particularly with anti-inflammatory,

anti-proliferative, immuno-suppressive, cytoprotective and antiviral activity. An example of such an inhibitor is 3,4-dichloroisocumarin.

ST NFkappaB inhibitor **heat shock** factor activator antiproliferative virucide

IT Transcription factors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HSF (**heat-shock** factor); inhibitors of the NF-κB factor as activators of HSF and inducers of **heat shock proteins** for antiproliferative and antiviral therapy)

IT **Heat-shock proteins**
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(**HSP 70**; inhibitors of the NF-κB factor as activators of HSF and inducers of **heat shock proteins** for antiproliferative and antiviral therapy)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**HSP70**; inhibitors of the NF-κB factor as activators of HSF and inducers of **heat shock proteins** for antiproliferative and antiviral therapy)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NF-κB (nuclear factor κB), inhibitors; inhibitors of the NF-κB factor as activators of HSF and inducers of **heat shock proteins** for antiproliferative and antiviral therapy)

IT Anti-inflammatory agents
Antiviral agents
Cytoprotective agents
Cytotoxic agents
DNA viruses
Human immunodeficiency virus 1
Immunosuppressants
Vesicular stomatitis virus
(inhibitors of the NF-κB factor as activators of HSF and inducers of **heat shock proteins** for antiproliferative and antiviral therapy)

IT Translation, genetic
(of **heat-shock** factors; inhibitors of the NF-κB factor as activators of HSF and inducers of **heat shock proteins** for antiproliferative and antiviral therapy)

IT Transcription, genetic
(of **heat-shock** genes; inhibitors of the NF-κB factor as activators of HSF and inducers of **heat shock proteins** for antiproliferative and antiviral therapy)

IT Proliferation inhibition
(proliferation inhibitors; inhibitors of the NF-κB factor as activators of HSF and inducers of **heat shock proteins** for antiproliferative and antiviral therapy)

IT RNA viruses
(single-stranded neg.-polarized; inhibitors of the NF-κB factor as activators of HSF and inducers of **heat shock proteins** for antiproliferative and antiviral therapy)

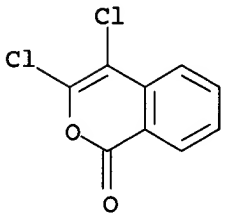
IT 402-71-1 2364-87-6 20874-31-1 **51050-59-0**, 3,4-**Dichloroisocoumarin** 219787-74-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)
(inhibitors of the NF-κB factor as activators of HSF and inducers of **heat shock proteins** for antiproliferative and antiviral therapy)

IT 37259-58-8, Serine **proteinase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; inhibitors of the NF-κB factor as activators of HSF and inducers of **heat shock proteins** for antiproliferative and antiviral therapy)

IT **51050-59-0**, 3,4-**Dichloroisocoumarin**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of the NF-κB factor as activators of HSF and inducers of **heat shock proteins** for antiproliferative and antiviral therapy)

RN 51050-59-0 HCAPLUS
CN 1H-2-Benzopyran-1-one, 3,4-dichloro- (9CI) (CA INDEX NAME)



L49 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1998:508719** HCAPLUS
DN **129:227391**
ED Entered STN: 17 Aug 1998
TI Protection from oxidative inactivation of the 20 S proteasome by **heat-shock protein 90**
AU Conconi, Mariangela; Petropoulos, Isabelle; Emod, Istvan; Turlin, Evelyne; Biville, Francis; Friguet, Bertrand
CS Unite de Biochimie Cellulaire, Institut Pasteur, Paris, 75724, Fr.
SO Biochemical Journal (**1998**), 333(2), 407-415
CODEN: BIJOAK; ISSN: 0264-6021
PB Portland Press Ltd.
DT Journal
LA English
CC 7-3 (Enzymes)
AB **Heat-shock protein 90** (**Hsp 90**) has been implicated in both protection against oxidative inactivation and inhibition of the multicatalytic **proteinase** (MCP, also known as 20 S proteasome). We report here that the protective and inhibitory effects of **Hsp 90** depend on the activation state of the proteasome. **Hsp 90** (and also α-crystallin) inhibits the N-Cbz-Leu-Leu-Leu-MCA-hydrolyzing activity (Cbz = benzyloxycarbonyl; MCA = 7-amido-4-**methylcoumarin**) when the rat liver MCP is in its latent form, but no inhibitory effects are observed when the MCP is in its active form. Metal-catalyzed oxidation of the active MCP inactivates the Ala-Ala-Phe-MCA-hydrolyzing (chymotrypsin-like), N-Boc-Leu-Ser-Thr-Arg-MCA-hydrolyzing (trypsin-like; Boc = t-butyloxycarbonyl), N-Cbz-Leu-Leu-Glu-β-naphthylamine-hydrolyzing (peptidylglutamyl-peptide hydrolase) and N-Cbz-Leu-Leu-Leu-MCA-hydrolyzing activities, whereas these activities are actually increased when the MCP is in its latent form. **Hsp 90** protects against oxidative inactivation of the trypsin-like and

N-Cbz-Leu-Leu-Leu-MCA-hydrolyzing activities of the MCP active form, and α-crystallin protects the trypsin-like activity. The specificity of the **Hsp 90**-mediated protection was assessed by a quant. anal. of the two-dimensional electrophoretic pattern of MCP subunits before and after oxidation of the MCP, in the presence or absence of **Hsp 90**. Treatment of the FAO hepatoma cell line with iron and ascorbate was found to inactivate the MCP. **Hsp 90** overexpression obtained by challenging the cells with iron was associated with a decreased susceptibility to oxidative inactivation of the MCP trypsin-like activity. Depletion of **Hsp 90** by using antisense oligonucleotides resulted in an increased susceptibility to oxidative inactivation of the MCP trypsin-like activity, providing evidence for the physiol. relevance of **Hsp 90**-mediated protection of the MCP.

ST multicatalytic **proteinase** oxidative inactivation **HSP90** ; proteasome alpha crystallin metal catalyzed oxidn

IT **Heat-shock proteins**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**HSP 90**; protection from oxidative inactivation of 20 S proteasome by **heat-shock protein 90**)

IT Crystallins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(α-; protection from oxidative inactivation of 20 S proteasome by **heat-shock protein 90**)

IT 140879-24-9, Multicatalytic **proteinase**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(20 S proteasome; protection from oxidative inactivation of 20 S proteasome by **heat-shock protein 90**)

RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD

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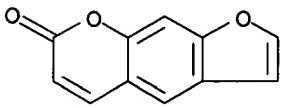
L49 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1996:363736** HCAPLUS
DN **125:52508**
ED Entered STN: 22 Jun 1996
TI Are stress **proteins** induced during PUVA therapy?
AU Al-Masaud, A. S.; Cunliffe, W. J.; Holland, D. B.
CS Skin Research Centre, University Leeds, Leeds, LS2 9JT, UK
SO British Journal of Dermatology (**1996**), 134(5), 892-899
CODEN: BJDEAZ; ISSN: 0007-0963
PB Blackwell
DT Journal
LA English
CC 8-9 (Radiation Biochemistry)
AB **Heat shock** or stress **proteins** are produced in practically all cell types when they are exposed to temps. a few degrees above normal. Measurement of the skin temperature of patients undergoing psoralen and UVA (PUVA) cabinet treatment for psoriasis revealed that the outer layers of the skin experience a mean temperature rise of 5-3°C. However, this did not produce a detectable stress response in epidermal samples taken after PUVA treatment. In vitro exposure of epidermis from biopsies or of cultured keratinocytes to a 5-7°C temperature rise produced a **heat shock** response, as measured by an increase in the production of **proteins** of the **HSP90** and **HSP70** families. These results were confirmed by the use of specific monoclonal antibodies. The corresponding mRNAs were also analyzed using labeled probes. In an in vitro system, following simulated PUVA treatment of cultured keratinocytes, increases in the synthesis of **HSP90** and **HSP70** were detected but these increases did not correlate with changes in mRNA levels.
ST psoralen UV stress **protein** psoriasis
IT Psoriasis
(stress **proteins** induced during PUVA therapy in humans)
IT Ultraviolet radiation
(A, stress **proteins** induced during PUVA therapy in humans)
IT **Proteins**, specific or class
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

(stress-induced, stress **proteins** induced during PUVA therapy in humans)

IT **66-97-7**, Psoralen
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stress **proteins** induced during PUVA therapy in humans)

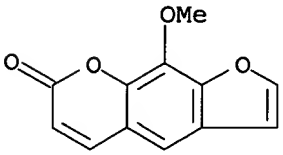
IT **66-97-7**, Psoralen
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stress **proteins** induced during PUVA therapy in humans)

RN 66-97-7 HCAPLUS
CN 7H-Furo[3,2-g][1]benzopyran-7-one (8CI, 9CI) (CA INDEX NAME)



L49 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1994:100699** HCAPLUS
DN **120:100699**
ED Entered STN: 05 Mar 1994
TI 8-Methoxypsoralen plus UVA induces the 72 kDa **heat shock protein** in organ-cultured normal human skin
AU Muramatsu, T.; Yamashina, Y.; Tada, H.; Kobayashi, N.; Yamaji, M.; Ohno, H.; Shirai, T.; Takahashi, A.; Ohinishi, T.
CS Dep. Dermatol., Nara Med. Univ., Kashihara, 634, Japan
SO Photochemistry and Photobiology (**1993**), 58(6), 809-12
CODEN: PHCBAP; ISSN: 0031-8655
DT Journal
LA English
CC 8-7 (Radiation Biochemistry)
AB The **proteins** induced by heat and other stressors, called **heat shock proteins** (**HSP**) or stress **proteins**, are considered to play a general role in protection from cellular injury. Exposure to UVA (320-400 nm) following application of 8-methoxypsoralen (8-MOP), termed PUVA is commonly used in the field of dermatol. To understand the induction of **HSP** in PUVA-treated human skin, indirect immunofluorescence using a monoclonal antibody specific for the 72 kDa **HSP** (**HSP** 72) was carried out in organ-cultured normal human skin that was treated with PUVA. When the organ-cultured skin was treated at 37° for 1 h with 8-MOP at a final concentration of 10 or 100 μg/mL and exposed to UVA (51.3 kJ/m2), nuclear immunofluorescence of **HSP** 72 was detected in the epidermal cells 12 h after UVA irradiation In contrast, the induction of **HSP** 72 was not detected either by UVA irradiation or 8-MOP treatment. These results suggest that PUVA treatment is one of the stressors for human skin, and DNA damage caused by PUVA induces **HSP** 72.
ST UVA methoxypsoralen **HSP** 72 **protein** skin
IT Skin, metabolism
(**HSP** 72 **protein** expression in human, methoxypsoralen and UVA radiation induction of)
IT Photosensitizers
(methoxypsoralen, of **HSP** 72 **protein** expression in human skin to UVA radiation)
IT Photodynamic action
(of methoxypsoralen, on **HSP** 72 **protein** expression in human skin with UVA radiation)

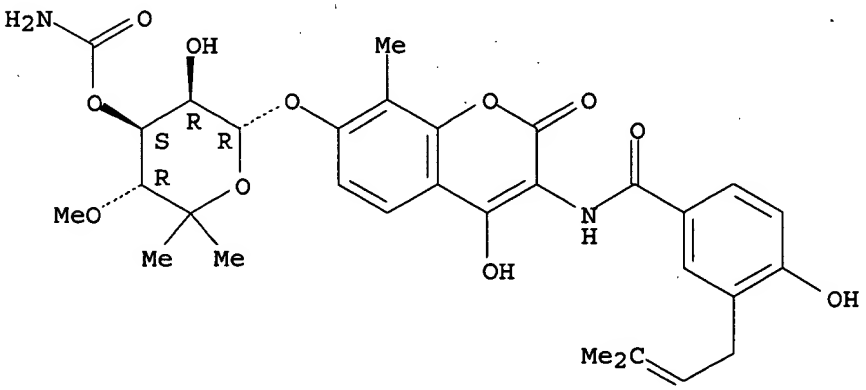
IT Ultraviolet radiation
(A, **HSP** 72 **protein** induction by methoxypsoralen and, in human skin)
IT **Proteins, specific or class**
RL: BIOL (Biological study)
(**HSP 72**, expression of, in human skin, methoxypsoralen and UVA radiation induction of)
IT **298-81-7**, 8-MOP
RL: BIOL (Biological study)
(**HSP** 72 **protein** induction by UVA radiation and, in human skin)
IT **298-81-7**, 8-MOP
RL: BIOL (Biological study)
(**HSP** 72 **protein** induction by UVA radiation and, in human skin)
RN 298-81-7 HCAPLUS
CN 7H-Furo[3,2-g][1]benzopyran-7-one, 9-methoxy- (8CI, 9CI) (CA INDEX NAME)



L49 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1994:95702** HCAPLUS
DN **120:95702**
ED Entered STN: 05 Mar 1994
TI **Heat shock** protection against induction of chromatid aberrations by triethylenemelamine in cultured human lymphocytes as affected by caffeine and **novobiocin**
AU Nicolova, Teodora; Petkova, Svetla
CS Inst. Ecol., Sofia, 1113, Bulg.
SO Biologisches Zentralblatt (**1993**), 112(4), 373-8
CODEN: BIZNAT; ISSN: 0006-3304
DT Journal
LA English
CC 1-12 (**Pharmacology**)
AB **Novobiocin** and caffeine modulation of protective effects triggered by **heat shock** (hs) against the clastogenic activity of the alkylating agent triethylenemelamine (TEM) in cultured human lymphocytes has been studied. **Heat shock** (hs; 15 min., 41°) prior to challenge treatment with TEM significantly reduced the frequency of metaphases with chromatid aberrations induced by TEM; **novobiocin** treatment before hs slightly reduced hs protection against the clastogen, while **novobiocin** application during the time span between hs and challenge treatment prevented hs-triggered protective effects. The application of caffeine after hs conditioning and before challenge treatment with TEM did not significantly affect hs protection, while caffeine posttreatment in G1 and G2 after hs and TEM-challenging dramatically increased the yield of TEM-induced chromatid aberrations, i.e., prevented any hs protection. Some considerations with respect to the time-limited nature of hs protection and the involvement of hs **proteins** and chromatin conformation in the hs response are discussed.
ST triethylenemelamine chromatid aberration lymphocyte **heat shock**; caffeine triethylenemelamine chromatid lymphocyte **heat shock**; **novobiocin** triethylenemelamine chromatid lymphocyte **heat shock**

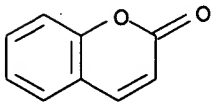
IT Chromatid
(aberrations, by triethylenemelamine in cultured human lymphocytes, **heat shock** protection against, caffeine and **novobiocin** modulation of)
IT Lymphocyte
(chromatid aberrations by triethylenemelamine in cultured human, **heat shock** protection against induction of, caffeine and **novobiocin** modulation of)
IT Shock
(heat, protection against induction of chromatid aberrations by triethylenemelamine in cultured human lymphocytes by, caffeine and **novobiocin** modulation of)
IT Drug interactions
(of caffeine and **novobiocin**, with **heat shock** protective effects against induction of chromatid aberrations by triethylenemelamine in cultured human lymphocytes)
IT Temperature effects, biological
(**heat, shock** from, protection against induction of chromatid aberrations by triethylenemelamine in cultured human lymphocytes by, caffeine and **novobiocin** modulation of)
IT 51-18-3, Triethylenemelamine
RL: BIOL (Biological study)
(chromatid aberrations by, in cultured human lymphocytes, **heat shock** protection against, caffeine and **novobiocin** modulation of)
IT 58-08-2, Caffeine, biological studies **303-81-1**, **Novobiocin**
RL: BIOL (Biological study)
(**heat shock** protection against induction of chromatid aberrations by triethylenemelamine in cultured human lymphocytes modulation by)
IT **303-81-1**, **Novobiocin**
RL: BIOL (Biological study)
(**heat shock** protection against induction of chromatid aberrations by triethylenemelamine in cultured human lymphocytes modulation by)
RN 303-81-1 HCAPLUS
CN Benzamide, N-[7-[[3-O-(aminocarbonyl)-6-deoxy-5-C-methyl-4-O-methyl-α-L-lyxo-hexopyranosyl]oxy]-4-hydroxy-8-methyl-2-oxo-2H-1-benzopyran-3-yl]-4-hydroxy-3-(3-methyl-2-butenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L49 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1992:528260** HCAPLUS
DN **117:128260**

ED Entered STN: 04 Oct 1992
TI Natural inhibitors of germination and growth. VI. Detection of a carboxy-terminal fragment of the **heat shock protein HSP** 70 after **coumarin** treatment
AU Oster, U.; Kardinal, C.; Burghardt, H.; Werner, B.; Lottspeich, F.; Ruediger, W.
CS Bot. Inst., Univ. Muenchen, Munich, D-8000/19, Germany
SO Journal of Plant Physiology (**1992**), 140(1), 110-15
CODEN: JPPHEY; ISSN: 0176-1617
DT Journal
LA English
CC 11-3 (Plant Biochemistry)
AB To elucidate the mechanism of germination inhibition by **coumarin**, **protein** patterns of dry seeds, seedlings germinated for 48 h, and **coumarin**-treated seeds from cress (Lepidium sativum) were investigated. The **coumarin**-treated seeds failed to germinate and showed a strong 32 kDa **protein** band that was not observed in germinated seedlings but was found in dry seeds. This **protein** was isolated, and the first 16 amino acids of the N-terminus were sequenced. The sequence showed a 100% identity with the amino acids 396-421 of the **heat-shock protein HSP** 70. Apparently, inhibition of **HSP** 70 proteolysis is involved in the inhibition of germination by **coumarin.**
ST **heat shock protein** cress germination; **coumarin** proteolysis germination inhibition
IT Germination
(**coumarin** inhibition of, **heat-shock protein HSP** 70 proteolysis in cress seeds in)
IT Seed
(**heat-shock protein** fragment of **coumarin**-treated, of cress)
IT Lepidium sativum
(**heat-shock protein** fragment of germination inhibitor-treated seeds of)
IT **Protein** sequences
(of **HSP** 70 fragment from **coumarin**-treated cress seed, N-terminus)
IT **Proteins, specific or class**
RL: BIOL (Biological study)
(**HSP 70**, proteolysis of, in cress seeds treated with germination inhibitor)
IT **91-64-5**, **2H-1-Benzopyran-2-one**
RL: BIOL (Biological study)
(germination inhibition by, **heat-shock HSP** 70 **protein** proteolysis in)
IT 143222-50-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
IT **91-64-5**, **2H-1-Benzopyran-2-one**
RL: BIOL (Biological study)
(germination inhibition by, **heat-shock HSP** 70 **protein** proteolysis in)
RN 91-64-5 HCAPLUS
CN 2H-1-Benzopyran-2-one (9CI) (CA INDEX NAME)



L49 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1988:626487** HCAPLUS
DN **109:226487**
ED Entered STN: 24 Dec 1988
TI **Heat-shock** response in Legionella pneumophila
AU Lema, Michael W.; Brown, Arnold; Butler, Charles A.; Hoffman, Paul S.
CS Res. Serv., W. J. B. Dorn Veterans Hosp., Columbia, SC, 29201, USA
SO Canadian Journal of Microbiology (**1988**), 34(10), 1148-53
CODEN: CJMIAZ; ISSN: 0008-4166
DT Journal
LA English
CC 10-2 (Microbial Biochemistry)
AB The **heat-shock** response of L. pneumophila was examined by radiolabeling bacterial cell **proteins** with [35S]methionine following a temperature shift from 30 to 42°. Five **heat-shock proteins** were identified as having mol. masses of 17, 60, 70, 78, and 85 kilodaltons (kDa). The 85- and 60-kDa **proteins** were equally distributed between supernatant and pellet fractions following ultracentrifugation at 100,000 + g, the 70- and 78-kDa **proteins** were found primarily in the supernatant, and the 17-kDa **protein** was found primarily in the pellet. Synthesis of subsets of the **heat-shock proteins** could be stimulated by **novobiocin**, patulin, or puromycin. EtOH, an effector of the **heat-shock** response in other microorganisms, had little effect on L. pneumophila, even at the highest concentration tolerated by the bacterial cells (1.9%). Finally, the 60-kDa **heat-shock protein** of L. pneumophila was immunol. cross-reactive with a polyclonal antibody prepared to the Escherichia coli groEL **protein.** However, a mouse monoclonal antibody reactive with the 60-kDa **protein** of all legionellae tested did not cross-react with the E. coli groEL **protein**, suggesting that the Legionella 60-kDa **protein** contains common and unique epitopes.
ST **heat shock protein** Legionella
IT Legionella pneumophila
(**heat-shock** response in)
IT **Proteins, specific or class**
RL: FORM (Formation, nonpreparative)
(**heat-shock**, formation of, by Legionella pneumophila)

L49 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1988:567088** HCAPLUS
DN **109:167088**
ED Entered STN: 12 Nov 1988
TI The role of **heat shock proteins** in differentiation of Trypanosoma brucei
AU Davis, Charles E.; Guiney, D. G.; Colmerauer, M. E. M.
CS Sch. Med., UCSD, San Diego, CA, 92103, USA
SO UCLA Symposia on Molecular and Cellular Biology, New Series (**1987**), 42(Mol. Strategies Parasit. Invasion), 169-79
CODEN: USMBD6; ISSN: 0735-9543
DT Journal
LA English
CC 10-3 (Microbial Biochemistry)
AB Near peak parasitemia, T. brucei differentiates from rapidly-replicating long-slender forms to short-stumpies that do not replicate in the mammal but are necessary to infect the tsetse. Indomethacin accelerates differentiation, whereas theophylline blocks the process, in association with changes in intratrypanosomal cAMP. In an attempt to find natural regulators and markers of differentiation, lysates of long-slenders,

short-stumpies and procyclics (insect mid-gut form) were probed for **heat-shock proteins** (**hsp**), because trypanosomes experience several temperature changes during their life cycle. Anti-chicken **hsp**-70 detected prominent 70 K dalton bands in immunoblots of each morphol. form. Furthermore, **novobiocin**, which blocks the **heat-shock** response of Drosophila, also blocks differentiation of T. brucei in mice. In 3 expts., T. brucei populations in treated mice never completely differentiated and mean parasitemia never remitted, whereas control mice experienced 2 cycles of parasitemia. Thus, differentiation of T. brucei, which moderates parasitemia and is essential to the life cycle, may be triggered by **hsp** induced by mammalian fever.

ST Trypanosoma differentiation **heat shock protein**

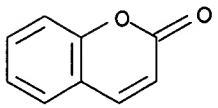
IT Trypanosoma brucei
(differentiation of, **heat-shock protein hsp70** in)

IT Microorganism development
(of Trypanosoma brucei, **heat shock protein hsp70** in relation to)

IT **Proteins, specific or class**
RL: BIOL (Biological study)
(**hsp 70**, in differentiation of Trypanosoma brucei)

L49 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1984:504070** HCAPLUS
DN **101:104070**
ED Entered STN: 29 Sep 1984
TI Teratogens induce a subset of small **heat shock proteins** in Drosophila primary embryonic cell cultures
AU Buzin, Carolyn H.; Bournias-Vardiabasis, Nicole
CS Div. Cytogenet. Cytol., City Hope Med. Cent., Duarte, CA, 91010, USA
SO Proceedings of the National Academy of Sciences of the United States of America (**1984**), 81(13), 4075-9
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
CC 1-12 (**Pharmacology**)
Section cross-reference(s): 2, 4, 12
AB Drosophila Embryonic cells placed into culture just after gastrulation differentiate in vitro over the next 24 h. A number of drugs that are teratogenic in mammalian systems have been found to inhibit muscle or neuron differentiation (or both) in these developing cultures. By two-dimensional gel electrophoresis, the effects of these drugs on **protein** synthesis in embryonic cells were examined For 9 teratogens tested, cells treated for 20 h with the drug show a dramatic induction of three **proteins** of about 20 kilodaltons, in addition to the normal **proteins** synthesized by untreated cells. Three teratogens as well as all 8 nonteratogens tested did not show this induction. The induced **proteins** appear to be identical to 3 or the **heat-shock proteins** (**hsp** 23, 22a, and 22b), as shown by electrophoresis mobilities and peptide mapping by partial proteolysis. A 37° **heat shock** of the embryonic cells produces the full complement of **heat-shock proteins**, whereas drug-treated cells induce only the subset **hsp** 23, 22a, and 22b but not **hsp** 26 or 27. β-Ecdysterone [5289-74-7], the Drosophila molting hormone, also inhibits embryonic differentiation and induces **hsp** 23, 22a, and 22b, a partial subset of the **heat shock proteins** (**hsp** 22, 23, 26, and 27) induced by the hormone in imaginal discs and some Drosophila continuous cell lines. Dose-response studies of several drugs show a correlation between the degree of inhibition of differentiation and the level of induction of **hsp** 23, 22a, and 22b: The induction of **heat**

shock proteins by drugs may reflect specific types of stress that can also give rise to teratogenesis.
ST teratogen Drosophila **heat shock protein**
IT Drosophila (insect)
(**heat-shock proteins** induction in embryonic cells of, by teratogens)
IT Teratogens
(Drosophila embryonic cell **heat shock protein** response to)
IT 50-02-2 50-49-7 53-06-5 56-53-1 57-41-0 57-83-0, biological studies 58-08-2, biological studies 58-18-4 59-05-2 60-80-0 63-74-1 64-17-5, biological studies 64-77-7 67-68-5, biological studies 76-74-4 81-07-2 **91-64-5** 320-67-2 915-67-3 5289-74-7
RL: BIOL (Biological study)
(Drosophila embryonic cell **heat shock protein** response to)
IT **91-64-5**
RL: BIOL (Biological study)
(Drosophila embryonic cell **heat shock protein** response to)
RN 91-64-5 HCAPLUS
CN 2H-1-Benzopyran-2-one (9CI) (CA INDEX NAME)



L49 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1983:65128** HCAPLUS
DN **98:65128**
ED Entered STN: 12 May 1984
TI The induction of a subset of **heat-shock proteins** by drugs that inhibit differentiation in Drosophila embryonic cell cultures
AU Buzin, Carolyn H.; Bournias-Vardiabasis, Nicole
CS Div. Cytogenet. Cytol., City of Hope Med. Cent., Duarte, CA, 91010, USA
SO Heat Shock: Bact. Man, [Pap. Meet.] (**1982**), 387-94. Editor(s): Schlesinger, Milton J.; Ashburner, Michael; Tissieres, Alfred. Publisher: Cold Spring Harbor Lab., Cold Spring Harbor, N. Y.
CODEN: 49ARAW
DT Conference
LA English
CC 1-4 (**Pharmacology**)
Section cross-reference(s): 2
AB In Drosophila primary embryonic cells, 8 of 10 drugs tested that inhibit differentiation stimulated formation of 3 **heat-shock proteins** with the same electrophoretic mobilities as **hsp23**, **hsp22a**, and **hsp22b proteins** but did not affect the formation of other **heat-shock proteins**; **heat shock** of the embryonic cells induced the full complement of **heat-shock proteins**. In contrast, 7 drugs that do not inhibit differentiation did not induce the 3 **proteins**. A mild heat treatment (that induces **heat-shock proteins**) partially protects cells from the inhibition of differentiation caused by a subsequent 2-h period of hyperthermia or drug treatment. Since the formation of a subset of **heat-shock proteins** can be separated from that of the entire complement of **heat-**

shock proteins, studies on the function and control of **hsp22** and **hsp23** can be carried out in the absence of the other **heat-shock proteins**. The **hsp23**, **hsp22a**, and **hsp22b proteins** may be involved in the protective effect of mild heat pretreatment.

ST drug embryo differentiation **protein** Drosophila; **heat shock protein** embryo drug

IT Drosophila (insect)
(embryonic cells of, **heat-shock proteins** induction by drugs and heat in, differentiation inhibition in relation to)

IT Embryo
(**heat-shock proteins** induction by drugs and heat in, of Drosophila, differentiation inhibition in relation to)

IT Heat, biological effects
(**heat-shock proteins** induction by, in embryonic cells of Drosophila, differentiation inhibition in relation to)

IT Pharmacology
(**heat-shock proteins** of embryonic cells of Drosophila response in, differentiation inhibition in relation to)

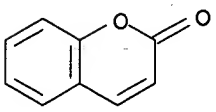
IT **Proteins**
RL: BIOL (Biological study)
(**heat-shock**, of embryonic cells of Drosophila, drugs and heat induction of, differentiation in relation to)

IT 50-02-2 53-06-5 56-53-1 57-41-0 57-83-0, biological studies 58-08-2, biological studies 58-18-4 59-05-2 60-80-0 63-74-1 64-77-7 67-68-5, biological studies 76-74-4 81-07-2 **91-64-5** 915-67-3 5289-74-7
RL: BIOL (Biological study)
(**heat-shock proteins** of embryonic cells of Drosophila response to, differentiation inhibition in relation to)

IT **91-64-5**
RL: BIOL (Biological study)
(**heat-shock proteins** of embryonic cells of Drosophila response to, differentiation inhibition in relation to)

RN 91-64-5 HCAPLUS

CN 2H-1-Benzopyran-2-one (9CI) (CA INDEX NAME)



L49 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

AN **1983:50260** HCAPLUS

DN **98:50260**

ED Entered STN: 12 May 1984

TI The **heat-shock** phenomenon in bacteria - a protection against DNA relaxation?

AU Travers, Andrew A.; Mace, Hilary A. F.

CS Lab. Mol. Biol., Med. Res. Counc. Cent., Cambridge, CB2 2QH, UK

SO Heat Shock: Bact. Man, [Pap. Meet.] (**1982**), 127-30. Editor(s): Schlesinger, Milton J.; Ashburner, Michael; Tissieres, Alfred. Publisher: Cold Spring Harbor Lab., Cold Spring Harbor, N. Y.
CODEN: 49ARAW

DT Conference

LA English

CC 10-5 (Microbial Biochemistry)

AB In organisms as diverse as Escherichia coli and humans, cells respond to

rapid temperature rises of 5-15° by inducing a transient production of **heat-shock proteins.** Also, agents that disrupt chromosomal structure might induce the synthesis of some or all **heat-shock proteins.** **Coumermycin** A1, an inhibitor of the B subunit of DNA topoisomerase II, induces the synthesis of a small set of **proteins** in E. coli cells sensitive to the drug. With 1 exception, all coumeromycin-induced **proteins** corresponded to **heat-shock proteins.** In Drosophila, gene **hsp70 heat-shock protein** appears to be associated with the interband regions of polytene chromosomes, suggesting that the **heat-shock protein** may also play a role in stabilizing chromosome structure in eukaryotes.

ST **heat shock protein** bacteria DNA relaxation

IT Bacteria
Escherichia coli
(**heat-shock proteins** of, DNA relaxation in relation to)

IT Deoxyribonucleic acids
RL: PROC (Process)
(relaxation of, in bacteria, **heat-shock protein** in relation to)

IT **Proteins**
RL: BIOL (Biological study)
(**heat-shock**, in bacteria, DNA relaxation in relation to)

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FILE 'BIOSIS' ENTERED AT 09:27:57 ON 12 AUG 2004
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CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 11 August 2004 (20040811/ED)

FILE RELOADED: 19 October 2003.
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     FILE 'HCAPLUS' ENTERED AT 09:24:50 ON 12 AUG 2004

     FILE 'BIOSIS' ENTERED AT 09:25:17 ON 12 AUG 2004
                E MARCU M/AU
L54          17 S E3,E9,E10
                E NECKERS L/AU
L55         301 S E3-E11
                E SCHULTE T/AU
L56          69 S E3,E8,E10-E12
L57         349 S L54-L56
L58          64 S (HSP? OR HEAT SHOCK) AND L57
L59          35 S ?CHAPERON? AND L57
L60          67 S L58,L59
L61           7 S L60 AND L9,L12,L13
L62           7 S L60 AND L19
L63           0 S L60 AND L20
L64           0 S L60 AND L21
L65           7 S L61,L62
L66           7 S L65 AND ?PROTEIN?
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L67 7 S L66 AND 90
L68 7 S L66-L67

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L69 7 S L68 AND L54-L68
E MARCU M/AU
L70 2 S E3,E4 AND L69
L71 11 S E3,E4 NOT L70
L72 7 S L69,L70

=> d all tot

L72 ANSWER 1 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:484752 BIOSIS
DN PREV200300484752
TI The C-terminal half of **heat shock protein 90** represents a second site for pharmacologic intervention in **chaperone** function.
AU **Marcu, Monica G.; Neckers, Leonard M.** [Reprint Author]
CS Cell and Cancer Biology Branch, Center for Cancer Research, National Cancer Institute, 9610 Medical Center Drive, Suite 300, Rockville, MD, 20850, USA
len@helix.nih.gov
SO Current Cancer Drug Targets, (October 2003) Vol. 3, No. 5, pp. 343-347. print.
ISSN: 1568-0096 (ISSN print).
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 15 Oct 2003
Last Updated on STN: 15 Oct 2003
CC Biochemistry studies - General 10060
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Enzymes - General and comparative studies: coenzymes 10802
Pathology - Therapy 12512
Pharmacology - General 22002
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Therapeutic agents and therapy 24008
IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Pharmacology; Tumor Biology
IT Diseases
cancer: neoplastic disease
Neoplasms (MeSH)
IT Chemicals & Biochemicals
cisplatin: antineoplastic-drug; **heat shock protein 90**: C-terminal, molecular **chaperone**; molybdate; **novobiocin**: enzyme inhibitor-drug; nucleotide; **protein** kinase [EC 2.7.1.37]; radicicol: antineoplastic-drug, enzyme inhibitor-drug; steroid receptors; transcription factors
IT Miscellaneous Descriptors
cell growth; cell survival
RN 15663-27-1 (cisplatin)
11116-47-5 (molybdate)
303-81-1 (novobiocin)
9026-43-1Q (**protein** kinase)
80449-02-1Q (**protein** kinase)
134549-83-0Q (**protein** kinase)
372092-80-3Q (**protein** kinase)
9026-43-1 (**protein** kinase)
9026-43-1Q (EC 2.7.1.37)
80449-02-1Q (EC 2.7.1.37)
134549-83-0Q (EC 2.7.1.37)

372092-80-3Q (EC 2.7.1.37)
9026-43-1 (EC 2.7.1.37)
12772-57-5 (radicicol)

L72 ANSWER 2 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:238051 BIOSIS
DN PREV200300238051
TI Development of small molecule **Hsp90** inhibitors: Utilizing both forward and reverse chemical genomics for drug identification.
AU **Neckers, Len** [Reprint Author]
CS Cell and Cancer Biology Branch, National Cancer Institute, NIH, 9610 Medical Center Drive, Suite 300, Rockville, MD, 20850, USA len@helix.nih.gov
SO Current Pharmaceutical Design, (May 2003) Vol. 10, No. 9, pp. 733-739. print.
ISSN: 1381-6128 (ISSN print).
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 14 May 2003
Last Updated on STN: 14 May 2003
CC Biochemistry studies - Proteins, peptides and amino acids 10064
Pathology - Therapy 12512
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Therapeutic agents and therapy 24008
IT Major Concepts
Pharmacology; Tumor Biology
IT Diseases
cancer: neoplastic disease
Neoplasms (MeSH)
IT Chemicals & Biochemicals
17-allylaminogeldanamycin [17-AAG]: antineoplastic-drug, phase I clinical trial; Akt; Bcr-Abl; HER2/Neu [ErbB2]; HIF-1-alpha; Raf-1; benzoquinone ansamycin; **heat shock protein 90 [Hsp90]**: carboxy-terminal ATP binding site, molecular **chaperone**; **novobiocin**: antineoplastic-drug, enzyme inhibitor-drug; p53; radicicol: antineoplastic-drug; small molecule **heat shock protein 90** inhibitors [small molecule **Hsp90** inhibitors]: antineoplastic-drug
IT Methods & Equipment
drug identification: laboratory techniques
IT Miscellaneous Descriptors
forward chemical genomics; reverse chemical genomics; signaling pathways
RN 75747-14-7 (17-allylaminogeldanamycin)
75747-14-7 (17-AAG)
303-81-1 (novobiocin)
12772-57-5 (radicicol)

L72 ANSWER 3 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2002:418975 BIOSIS
DN PREV200200418975
TI Curcumin, an antioxidant and anti-inflammatory phytochemical, depletes **Hsp90**-dependent signaling **proteins** without direct binding to the **chaperone.**
AU **Marcu, Monica G.** [Reprint author]; **Neckers, Len** [Reprint author]
CS NIH, NCI, Rockville, MD, USA
SO Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2002) Vol. 43, pp. 964. print.

Meeting Info.: 93rd Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA. April 06-10, 2002.
ISSN: 0197-016X.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 7 Aug 2002
Last Updated on STN: 7 Aug 2002
CC General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - Proteins, peptides and amino acids 10064
Pathology - Therapy 12512
Metabolism - General metabolic pathways 13002
Pharmacology - General 22002
Pharmacology - Drug metabolism and metabolic stimulators 22003
Pharmacology - Connective tissue, bone and collagen-acting drugs 22012
Pharmacology - Immunological processes and allergy 22018
Chemotherapy - General, methods and metabolism 38502
IT Major Concepts
Metabolism; Pharmacology
IT Chemicals & Biochemicals
ATP; Akt: **heat shock protein 90** -dependent kinase, regulation; ErbB2: **heat shock protein 90**-dependent kinase, regulation; Raf1: **heat shock protein 90**-dependent kinase, regulation; **chaperone protein**: binding; curcumin: antiinflammatory-drug, immunologic-drug, metabolic-drug, pharmacodynamics; geldanamycin: antiinfective-drug; **heat shock protein 90 [Hsp90]**; **novobiocin**: antiinfective-drug, enzyme inhibitor-drug; p53: mutation, regulation; signaling **protein**: regulation
IT Miscellaneous Descriptors
Meeting Abstract
RN 56-65-5Q (ATP)
42530-29-0Q (ATP)
94587-45-8Q (ATP)
111839-44-2Q (ATP)
458-37-7 (curcumin)
30562-34-6 (geldanamycin)
303-81-1 (novobiocin)

L72 ANSWER 4 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2001:48490 BIOSIS
DN PREV200100048490
TI The **heat shock protein 90** antagonist **novobiocin** interacts with a previously unrecognized ATP-binding domain in the carboxyl terminus of the **chaperone**.
AU **Marcu, Monica G.**; Chadli, Ahmed; Bouhouche, Ilham; Catelli, Maria; **Neckers, Leonard M.** [Reprint author]
CS Department of Cell and Cancer Biology, Medicine Branch, NCI, National Institutes of Health, Rockville, MD, 20850, USA
len@helix.nih.gov
SO Journal of Biological Chemistry, (November 24, 2000) Vol. 275, No. 47, pp. 37181-37186. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DT Article
LA English
ED Entered STN: 24 Jan 2001
Last Updated on STN: 12 Feb 2002
AB **Heat shock protein 90** (**Hsp90**), one of the most abundant **chaperones** in eukaryotes, participates in folding and stabilization of signal-transducing molecules including steroid hormone receptors and

protein kinases. The amino terminus of **Hsp90** contains a non-conventional nucleotide-binding site, related to the ATP-binding motif of bacterial DNA gyrase. The anti-tumor agents geldanamycin and radicicol bind specifically at this site and induce destabilization of **Hsp90** -dependent client **proteins.** We recently demonstrated that the gyrase inhibitor **novobiocin** also interacts with **Hsp90**, altering the affinity of the **chaperone** for geldanamycin and radicicol and causing in vitro and in vivo depletion of key regulatory **Hsp90**-dependent kinases including v-Src, Raf-1, and p185ErbB2. In the present study we used deletion/mutation analysis to identify the site of interaction of **novobiocin** with **Hsp90**, and we demonstrate that the **novobiocin**-binding site resides in the carboxyl terminus of the **chaperone.** Surprisingly, this motif also recognizes ATP, and ATP and **novobiocin** efficiently compete with each other for binding to this region of **Hsp90.** **Novobiocin** interferes with association of the co-**chaperones** Hsc70 and p23 with **Hsp90.** These results identify a second site on **Hsp90** where the binding of small molecule inhibitors can significantly impact the function of this **chaperone**, and they support the hypothesis that both amino- and carboxyl-terminal domains of **Hsp90** interact to modulate **chaperone** activity.

CC Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - General 10060
Enzymes - General and comparative studies: coenzymes 10802
Pathology - Therapy 12512
Pharmacology - General 22002
Neoplasms - Therapeutic agents and therapy 24008

IT Major Concepts
Biochemistry and Molecular Biophysics; Pharmacology

IT Chemicals & Biochemicals
ATP; DNA gyrase; Hsc70; geldanamycin: antineoplastic-drug; **heat shock protein 90**; molecular **chaperone**: ATP-binding domain; **novobiocin**: enzyme inhibitor; p23; radicicol: antineoplastic-drug

IT Miscellaneous Descriptors
protein-drug interaction; signal transduction

RN 56-65-5Q (ATP)
42530-29-0Q (ATP)
94587-45-8Q (ATP)
111839-44-2Q (ATP)
30562-34-6 (geldanamycin)
303-81-1 (novobiocin)
12772-57-5 (radicicol)

L72 ANSWER 5 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2000:252235 BIOSIS
DN PREV200000252235
TI **Novobiocin**, a **heat shock protein 90** (**HSP90**) inhibitor, interacts with a previously uncharacterized ATP-binding domain in the C-terminus of the **chaperone.**
AU **Marcu, M. G.** [Reprint author]; **Neckers, L. M.** [Reprint author]
CS National Cancer Inst, Rockville, MD, USA
SO Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2000) No. 41, pp. 312. print.
Meeting Info.: 91st Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA. April 01-05, 2000.
ISSN: 0197-016X.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English

ED Entered STN: 14 Jun 2000
Last Updated on STN: 5 Jan 2002
CC Neoplasms - General 24002
Biochemistry studies - General 10060
Pharmacology - General 22002
IT Major Concepts
Pharmacology; Tumor Biology
IT Chemicals & Biochemicals
ATP: binding affinity; geldanamycin: antineoplastic-drug; **heat shock protein-90**: C-terminus, **chaperone**; **novobiocin**: **heat shock protein-90** inhibitor
IT Methods & Equipment
deletion/mutation analysis: detection method
IT Miscellaneous Descriptors
Meeting Abstract
RN 56-65-5Q (ATP)
42530-29-0Q (ATP)
94587-45-8Q (ATP)
111839-44-2Q (ATP)
30562-34-6 (geldanamycin)
303-81-1 (**novobiocin**)

L72 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2000:100786 BIOSIS
DN PREV200000100786
TI **Novobiocin** and related **coumarins** and depletion of **heat shock protein 90**-dependent signaling **proteins.**
AU **Marcu, Monica G.**; **Schulte, Theodore W.**; **Neckers, Leonard** [Reprint author]
CS National Cancer Institute, 9610 Medical Center Dr., Suite 300, Rockville, MD, 20850, USA
SO Journal of the National Cancer Institute (Bethesda), (Feb. 2, 2000) Vol. 92, No. 3, pp. 242-248. print.
CODEN: JNCIEQ. ISSN: 0027-8874.
DT Article
LA English
ED Entered STN: 15 Mar 2000
Last Updated on STN: 3 Jan 2002
AB Background: **Heat shock protein 90** (**Hsp90**) interacts with and stabilizes several oncogenic **protein** kinases (e.g., p185erbB2, p60v-src, and Raf-1) and is required for the stability and dominant-negative function of mutated p53 **protein.** Two unrelated antibiotics, geldanamycin and radicicol, bind specifically to an atypical nucleotide-binding pocket of **Hsp90**, a site that shares homology with the adenosine triphosphate (ATP)-binding domain of bacterial DNA gyrase B. This interaction leads to destabilization of **proteins** that interact with **Hsp90.** Since the nucleotide-binding site of gyrase B is targeted by **coumarin** antibiotics (e.g., **novobiocin**), we investigated whether these drugs can also interact with **Hsp90** and affect its activity. Methods: We used immobilized **novobiocin**, geldanamycin, or radicicol to isolate either endogenous **Hsp90** from cell lysates or **Hsp90** deletion fragments translated in vitro. Effects of the **coumarin** antibiotics **novobiocin** , **chlorobiocin**, and **coumermycin** A1 on several **proteins** interacting with **Hsp90** were assessed in vitro and in vivo. Results: **Hsp90** binding to immobilized **novobiocin** was competed by soluble **coumarins** and ATP but not by geldanamycin or radicicol. A carboxy-terminal **Hsp90** fragment bound immobilized **novobiocin** but not immobilized geldanamycin, while a geldanamycin-binding amino-terminal fragment did not

bind **novobiocin.** All three **coumarins** markedly reduced cellular levels of p185erbB2, p60v-src, Raf-1, and mutated p53. Furthermore, **novobiocin** reduced Raf-1 levels in the spleens of mice treated with the drug. Conclusions: These **coumarin** antibiotics, particularly **novobiocin**, represent a first-generation alternative to other **Hsp90**-targeting drugs that are not as well tolerated. **Novobiocin**'s unique interaction with **Hsp90** identifies an additional site on this **protein** amenable to pharmacologic interference with small molecules.

CC Pharmacology - General 22002
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - General 10060

IT Major Concepts
Biochemistry and Molecular Biophysics; Pharmacology

IT Chemicals & Biochemicals
Raf-1; **chlorobiocin**; **coumermycin** A1; geldanamycin; **heat shock protein 90**; **novobiocin**; p185-erbB2; p53; p60-v-src; radicicol

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

RN **39868-96-7** (**chlorobiocin**)
4434-05-3 (**coumermycin** A1)
30562-34-6 (geldanamycin)
303-81-1 (**novobiocin**)
12772-57-5 (radicicol)

L72 ANSWER 7 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1999:187460 BIOSIS
DN PREV199900187460
TI **Novobiocin** and other **coumarin** antibiotics bind to **Hsp90** and cause the degradation of **Hsp90**-dependent signaling **proteins.**
AU **Marcu, M. G.; Schulte, T. W.; Neckers, L. M.**
CS Med. Branch, NCI, Rockville, MD 20850, USA
SO Proceedings of the American Association for Cancer Research Annual Meeting, (March, 1999) Vol. 40, pp. 724. print.
Meeting Info.: 90th Annual Meeting of the American Association for Cancer Research. Philadelphia, Pennsylvania, USA. April 10-14, 1999. American Association for Cancer Research.
ISSN: 0197-016X.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 5 May 1999
Last Updated on STN: 5 May 1999
CC Neoplasms - General 24002
Biochemistry studies - General 10060
Biophysics - General 10502
Enzymes - General and comparative studies: coenzymes 10802
Pharmacology - General 22002
General biology - Symposia, transactions and proceedings 00520

IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Pharmacology; Tumor Biology

IT Diseases
cancer: neoplastic disease

Neoplasms (MeSH)
IT Chemicals & Biochemicals
novobiocin: **coumarin** antibiotic; **Hsp90** inhibitor [**heat shock protein-90** inhibitor]: antineoplastic activity, enzyme inhibitor
IT Miscellaneous Descriptors
drug-**protein** interaction: biochemical characterization; Meeting Abstract
RN **303-81-1** (**novobiocin**)
91-64-5 (**COUMARIN**)

=> => fil medline
FILE 'MEDLINE' ENTERED AT 09:37:55 ON 12 AUG 2004

FILE LAST UPDATED: 11 AUG 2004 (20040811/UP). FILE COVERS 1951 TO DATE.

On February 29, 2004, the 2004 MeSH terms were loaded. See HELP RLOAD for details. OLDMEDLINE now back to 1951.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a description of changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot

L83 ANSWER 1 OF 3 MEDLINE on STN
AN 1998324903 MEDLINE
DN PubMed ID: 9657982
TI Protection from oxidative inactivation of the 20S proteasome by **heat-shock protein 90.**
AU Conconi M; Petropoulos I; Emod I; Turlin E; Biville F; Friguet B
CS Unite de Biochimie Cellulaire, Institut Pasteur, 28 rue du Dr. Roux, 75724 Paris Cedex 15, France.
SO Biochemical journal, (**1998 Jul 15**) 333 (Pt 2) 407-15.
Journal code: 2984726R. ISSN: 0264-6021.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199809
ED Entered STN: 19980917
Last Updated on STN: 20000303
Entered Medline: 19980910
AB **Heat-shock protein 90** (**Hsp 90**) has been implicated in both protection against oxidative inactivation and inhibition of the multicatalytic proteinase (MCP, also known as 20 S proteasome). We report here that the protective and inhibitory effects of **Hsp 90** depend on the activation state of the proteasome. **Hsp 90** (and also alpha-crystallin) inhibits the N-Cbz-Leu-Leu-Leu-MCA-hydrolysing activity (Cbz=benzyloxycarbonyl; MCA=7-amido-4-**methylcoumarin**) when the rat liver MCP is in its latent form, but no inhibitory effects are observed when the MCP is in its active form. Metal-catalysed oxidation of the active MCP inactivates the Ala-Ala-Phe-MCA-hydrolysing (chymotrypsin-like), N-Boc-Leu-Ser-Thr-Arg-MCA-hydrolysing (trypsin-like; Boc=t-butyloxycarbonyl), N-Cbz-Leu-Leu-Glu-beta-naphthylamine-hydrolysing (peptidylglutamyl-peptide hydrolase) and N-Cbz-Leu-Leu-Leu-MCA-hydrolysing activities, whereas these activities are actually increased when the MCP

is in its latent form. **Hsp 90** protects against oxidative inactivation of the trypsin-like and N-Cbz-Leu-Leu-Leu-MCA-hydrolysing activities of the MCP active form, and alpha-crystallin protects the trypsin-like activity. The specificity of the **Hsp 90**-mediated protection was assessed by a quantitative analysis of the two-dimensional electrophoretic pattern of MCP subunits before and after oxidation of the MCP, in the presence or absence of **Hsp 90**. Treatment of the FAO hepatoma cell line with iron and ascorbate was found to inactivate the MCP. **Hsp 90** overexpression obtained by challenging the cells with iron was associated with a decreased susceptibility to oxidative inactivation of the MCP trypsin-like activity. Depletion of **Hsp 90** by using antisense oligonucleotides resulted in an increased susceptibility to oxidative inactivation of the MCP trypsin-like activity, providing evidence for the physiological relevance of **Hsp 90** -mediated protection of the MCP.

CT Check Tags: Male; Support, Non-U.S. Gov't
Animals
Ascorbic Acid: ME, metabolism
Catalysis
Cells, Cultured
Crystallins: ME, metabolism
*Cysteine Endopeptidases: ME, metabolism
Endopeptidases: ME, metabolism
***Heat-Shock Proteins 90: ME, metabolism**
Iron: ME, metabolism
Metals: ME, metabolism
*Multienzyme Complexes: ME, metabolism
Oligonucleotides, Antisense: ME, metabolism
Oligopeptides: ME, metabolism
Oxidation-Reduction
*Oxidative Stress
Rats
Rats, Inbred F344

RN 10329-75-6 (leucyl-leucyl-leucine); 50-81-7 (Ascorbic Acid); 7439-89-6 (Iron)

CN 0 (Crystallins); 0 (**Heat-Shock Proteins 90**); 0 (Metals); 0 (Multienzyme Complexes); 0 (Oligonucleotides, Antisense); 0 (Oligopeptides); EC 3.4.- (Endopeptidases); EC 3.4.22 (Cysteine Endopeptidases); EC 3.4.25.1 (proteasome endopeptidase complex)

L83 ANSWER 2 OF 3 MEDLINE on STN
AN **95257116** MEDLINE
DN PubMed ID: **7738787**
TI Thermally-induced cell lysis in Escherichia coli K12.
AU Membrillo-Hernandez J; Nunez-de la Mora A; del Rio-Albrechtsen T; Camacho-Carranza R; Gomez-Eichelmann M C
CS Instituto de Investigaciones Biomedicas, Universidad Nacional Autonoma de Mexico, D.F., Mexico.
SO Journal of basic microbiology, **(1995)** 35 (1) 41-6.
Journal code: 8503885. ISSN: 0233-111X.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199506
ED Entered STN: 19950615
Last Updated on STN: 19950615
Entered Medline: 19950607
AB Escherichia coli cells exposed to high temperatures exhibit a progressive loss of viability. We observed two mechanisms of cell death induced by lethal temperatures: with and without lysis. The number of cells lysed by heat decreased at later stages of the growth curve, when cells were

pre-treated at lower temperatures for 10 minutes and when cells were pre-treated with **novobiocin**, nalidixic acid and cadmium chloride. Cell lysis was similar in wild type, rpoH, groE and dnaK mutant cells as well as in cells which overproduce **heat shock proteins** GroE or DnaK. Results using cells aligned for cell division and cells growing at 42 degrees C, 45 degrees C and 47 degrees C suggest that cells near division are more sensitive to lysis and that a high concentration of **heat-shock proteins** increases their resistance to lysis.

CT Check Tags: Support, Non-U.S. Gov't
Cadmium: PD, pharmacology
Cadmium Chloride
Cell Division: DE, drug effects
Chlorides: PD, pharmacology
*Escherichia coli: CY, cytology
Escherichia coli: DE, drug effects
Escherichia coli: GE, genetics
Genes, Bacterial
GroEL Protein: BI, biosynthesis
GroEL Protein: GE, genetics
GroES Protein: BI, biosynthesis
GroES Protein: GE, genetics
Heat
Heat-Shock Proteins 70: BI, biosynthesis
Heat-Shock Proteins 70: GE, genetics
Mutation
Nalidixic Acid: PD, pharmacology
Novobiocin: PD, pharmacology

RN 10108-64-2 (Cadmium Chloride); **303-81-1 (Novobiocin)**; 389-08-2 (Nalidixic Acid); 7440-43-9 (Cadmium)

CN 0 (Chlorides); 0 (GroEL Protein); 0 (GroES Protein); 0 (**Heat-Shock Proteins** 70); EC 3.6.1.- (dnaK protein, E coli)

GEN dnaK; groE; rpoH

L83 ANSWER 3 OF 3 MEDLINE on STN

AN **85237507** MEDLINE

DN PubMed ID: **2989538**

TI **Novobiocin** blocks the Drosophila heat shock response.

AU Han S; Udvardy A; Schedl P

SO Journal of molecular biology, **(1985 May 5)** 183 (1) 13-29. Journal code: 2985088R. ISSN: 0022-2836.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 198508

ED Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19850801

AB In the studies reported here we show that the antibiotic **novobiocin**, an in vitro inhibitor of topoisomerase II, blocks the Drosophila heat shock response. If **novobiocin** is added prior to induction, there is no detectable expression of the Drosophila heat shock genes. Moreover, analysis of the chromatin organization of the 87A7 heat shock locus indicates that the antibiotic prevents the structural alterations which normally accompany heat induction. When **novobiocin** is added after induction, transcription appears to be rapidly turned off, and the chromatin organization of the 87A7 locus is "fixed" in an "active" configuration. **Novobiocin** also prevents the re-establishment of the pre-induced 87A7 chromatin organization which occurs during recovery from heat shock. We have also presented data suggesting that this antibiotic blocks transcription at 25 degrees C. These findings raise the possibility that topoisomerase II may be required

in eukaryotes for both gene activation and deactivation.
CT Check Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Aspergillus Nuclease S1
Autoradiography
Chromatin: DE, drug effects
Deoxyribonucleases
Drosophila: GE, genetics
Endonucleases
*Gene Expression Regulation: DE, drug effects
Genes: DE, drug effects
Heat
***Heat-Shock Proteins: GE, genetics**
Micrococcal Nuclease
Neurospora crassa: EN, enzymology
***Novobiocin: PD, pharmacology**
RNA, Messenger: BI, biosynthesis
RN **303-81-1 (Novobiocin)**
CN 0 (Chromatin); 0 (**Heat-Shock Proteins**); 0
(RNA, Messenger); EC 3.1.- (Deoxyribonucleases); EC 3.1.- (Endonucleases);
EC 3.1.30.1 (Aspergillus Nuclease S1); EC 3.1.31.1 (Micrococcal Nuclease)

=> => fil wpix
FILE 'WPIX' ENTERED AT 09:42:50 ON 12 AUG 2004
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FILE LAST UPDATED: 10 AUG 2004 <20040810/UP>
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NEW FORMAT GERMAN PATENT APPLICATION AND PUBLICATION
NUMBERS. SEE ALSO:
http://www.stn-international.de/archive/stnews/news0104.pdf <<<

=> d his

(FILE 'HOME' ENTERED AT 09:01:18 ON 12 AUG 2004)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 09:01:33 ON 12 AUG 2004
E COUMARIN/CN
L1 1 S E3
E NOVOBIOCIN/CN
L2 1 S E3
E CHLOROBIOCIN/CN

```
L3            1 S E3
                E HYDROXYCOUMARIN/CN
L4            1 S E3
                E DICUMAROL/CN
L5            1 S E3
                E WARFARIN/CN
L6            1 S E3
                E PHENPROCOUMON/CN
L7            1 S E3
                E COUMERMYCIN/CN
L8            1 S E3
L9            8 S L1-L8
                SEL RN
L10         213 S E1-E8/CRN
L11         130 S L10 NOT (PMS OR IDS OR MXS OR MNS)/CI
L12          21 S L11 NOT (COMPD OR WITH OR UNSPECIFIED OR CONJUGATE)
L13         192 S L10 NOT L12
L14       10774 S COUMARIN OR NOVOBIOCIN OR CHLOROBIOCIN OR HYDROXYCOUMARIN OR
L15       10680 S L14 NOT L9,L10

     FILE 'HCAPLUS' ENTERED AT 09:05:11 ON 12 AUG 2004
L16       14477 S L9 OR L12
L17         219 S L13
L18       33774 S L15
L19       42695 S ?COUMARIN? OR ?NOVOBIOCIN? OR ?CHLOROBIOCIN? OR ?HYDROXYCOUMA
L20        1187 S COUMADIN? OR 2H 1 BENZOPYRAN 2 ONE
L21        1146 S DICOUMAROL
L22       57132 S L16-L21
                E HEAT SHOCK PROTEIN/CT
L23       21562 S HEAT SHOCK(L)PROTEIN
                E HEAT-SHOCK/CT
L24        1699 S E62-E65
L25        9914 S E32-E61,E66-E68
                E E32+ALL
L26       15973 S E3-E6,E2+NT
                E HSP90
L27        2401 S E3-E19
L28           5 S E34
L29        3101 S HSP90 OR HSP 90
                E CHAPERONE/CT
                E E4+ALL
                E E2+ALL
L30        6435 S E3,E4,E2+NT
                E CHAPERONIN/CT
L31        2560 S E6-E12
                E E6+ALL
L32       11816 S CHAPERON?
L33          90 S L22 AND L23-L32
L34          51 S L33 AND (PD<=19990312 OR PRD<=19990312 OR AD<=19990312)
                E MARCU M/AU
L35          65 S E3,E4,E16,E17
                E MECKERS L/AU
                E NECKERS L/AU
L36         220 S E3-E8
                E SCHULTE T/AU
L37          37 S E3,E7,E9-E13
L38           4 S L33 AND L35-L37
L39           1 S L34 AND L38
L40           4 S L38,L39
L41          50 S L34 NOT L40
L42           7 S L41 AND (PHARMACEUT? OR PHARMACOL?)/SC,SX
                SEL DN AN 2 5 6 7 L42
L43           4 S L42 AND E1-E12
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L44          43 S L41 NOT L42
                SEL DN AN L44 5 19 30 33 36 37 43
L45           7 S L44 AND E13-E33
L46          15 S L40,L43,L45 AND L16-L45
L47          15 S L46 AND (HSP? OR HEAT SHOCK OR ?PROTEIN? OR 90)
L48           3 S L47 AND ?CHAPERON?
L49          15 S L47,L48
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 09:23:40 ON 12 AUG 2004
L50           7 S E34-E40
L51           3 S L50 AND L9,L12
L52           4 S L50 AND L13,L15
L53          12 S L9,L50-L52

     FILE 'REGISTRY' ENTERED AT 09:24:39 ON 12 AUG 2004

     FILE 'HCAPLUS' ENTERED AT 09:24:50 ON 12 AUG 2004

     FILE 'BIOSIS' ENTERED AT 09:25:17 ON 12 AUG 2004
                E MARCU M/AU
L54          17 S E3,E9,E10
                E NECKERS L/AU
L55         301 S E3-E11
                E SCHULTE T/AU
L56          69 S E3,E8,E10-E12
L57         349 S L54-L56
L58          64 S (HSP? OR HEAT SHOCK) AND L57
L59          35 S ?CHAPERON? AND L57
L60          67 S L58,L59
L61           7 S L60 AND L9,L12,L13
L62           7 S L60 AND L19
L63           0 S L60 AND L20
L64           0 S L60 AND L21
L65           7 S L61,L62
L66           7 S L65 AND ?PROTEIN?
L67           7 S L66 AND 90
L68           7 S L66-L67

     FILE 'BIOSIS' ENTERED AT 09:27:57 ON 12 AUG 2004
L69           7 S L68 AND L54-L68
                E MARCU M/AU
L70           2 S E3,E4 AND L69
L71          11 S E3,E4 NOT L70
L72           7 S L69,L70

     FILE 'MEDLINE' ENTERED AT 09:30:32 ON 12 AUG 2004
L73       12734 S L9,L12,L13
L74       27061 S L19,L20,L21
L75       27061 S L73,L74
                E HEAT SHOCK/CT
                E E13=ALL
                E HEAT SHOCK/CT
                E E13+ALL
                E E2+ALL
L76       12992 S E8+NT
                E E8+ALL
L77          38 S L75 AND L76
L78          76 S L75 AND (HSP? OR HEAT SHOCK (L) PROTEIN OR ?CHAPERON?)
L79          40 S L77,L78 AND PY<=1999
L80           2 S L79 AND (HSP90 OR HSP 90 OR 90)
L81           1 S L80 AND 90/TI
                SEL DN AN L79 23 38
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L82           2 S E1-E4
L83           3 S L81,L82 AND L73-L82

     FILE 'MEDLINE' ENTERED AT 09:37:55 ON 12 AUG 2004

     FILE 'WPIX' ENTERED AT 09:38:03 ON 12 AUG 2004
                E HSP/BI,ABEX
L84         146 S E105-E111
L85         121 S ((HSP OR HEAT SHOCK PROTEIN)(S)90)/BIX
L86         782 S HEAT SHOCK PROTEIN/BIX
L87         381 S ?CHAPERON?/BIX
L88        1154 S L84-L87
L89        4292 S L19/BIX OR L20/BIX OR L21/BIX
                E COUMARIN/DCN
                E E3+ALL
L90         331 S E2
                E NOVOBIOCIN/DCN
                E E3+ALL
L91          65 S E2 OR 1214/DRN
L92          39 S E4
                E CHLOROBIOCIN/DCN
                E HYDROXYCOUMARIN/DCN
                E E4+ALL
L93         212 S E2 OR 0487/DRN
L94          15 S E4
L95          51 S E6
L96           3 S E8
                E DICUMAROL/DCN
                E E3+ALL
L97          28 S E2 OR 0264/DRN
                E WARFARIN/DCN
                E E3+ALL
L98         212 S E2 OR 0487/DRN
L99          19 S E4
                E PHENPROCOUMON/DCN
                E E3+ALL
L100         11 S E2 OR 1253/DRN
                E COUMERMYCIN/DCN
                E E4+ALL
L101         12 S E2
L102         10 S L88 AND L89-L101

     FILE 'WPIX' ENTERED AT 09:42:50 ON 12 AUG 2004

=> d all l102 ab tech abex tot

L102 ANSWER 1 OF 10  WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN   2004-506948 [48]    WPIX
DNN  N2004-400584        DNC C2004-187639
TI   Radially expandable modular stent useful in the treatment of restenosis
     includes two stent modules forming two passageways; and polymer bridge
     between the stent modules such that both passageways are in fluid
     communication.
DC   A96 B05 B07 D22 P32
IN   KANTOR, J
PA   (MEDT) MEDTRONIC VASCULAR
CYC  98
PI   WO 2004052237   A2 20040624 (200448)* EN   26    A61F000-00
        RW: AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PT RO
            SE SI SK TR
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
            KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
```

RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW

ADT WO 2004052237 A2 WO 2003-US39290 20031209
PRAI US 2002-432278P 20021209
IC ICM A61F000-00
AB WO2004052237 A UPAB: 20040728
NOVELTY - A radially expandable modular stent (A1) includes a first stent module (F1) forming a first passageway; at least a second stent module (S1) forming at least a second passageway; and at least one polymer bridge (P1) in communication with (F1) and (S1). (P1) Couples (F1) to (S1) such that both passageways are in fluid communication.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for manufacturing (M1) of (A1) involving forming (F1) and (S1) from at least one stent material, and coupling (S1) to (F1) with (P1).

ACTIVITY - Vasotropic.

MECHANISM OF ACTION - None given.

USE - In vascular devices for implantation within the body of patients (claimed) during the treatment of restenosis.

ADVANTAGE - The polymeric coating containing therapeutic drugs provides controlled release of the drug in the localized environment, and contributes to great versatility of the vascular devices. The modular stents provide radially expanding force or support to a luminal structure; exhibit improved flexibility; and have decreased potential to module compaction.

Dwg.0/10
FS CPI GMPI
FA AB; DCN
MC CPI: A12-V02; A12-V03; B01-A01; B01-A02; B04-C01; B04-C01A; B04-C01B; B04-C02A; B04-C02B; B04-C02E; B04-C02E1; B04-C03; B04-H06; B04-H06B; B04-H06F; B04-H06J; B04-N04; B05-A03B; B05-C03; B06-A01; B06-A03; B06-D09; B06-E03; B06-E05; B07-D12; B08-C01; B10-A10; B10-A15; B10-C03; B10-C04D; B10-D01; B14-F01G; D09-C01; D09-C04
AB WO2004052237 A UPAB: 20040728
NOVELTY - A radially expandable modular stent (A1) includes a first stent module (F1) forming a first passageway; at least a second stent module (S1) forming at least a second passageway; and at least one polymer bridge (P1) in communication with (F1) and (S1). (P1) Couples (F1) to (S1) such that both passageways are in fluid communication.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for manufacturing (M1) of (A1) involving forming (F1) and (S1) from at least one stent material, and coupling (S1) to (F1) with (P1).

ACTIVITY - Vasotropic.

MECHANISM OF ACTION - None given.

USE - In vascular devices for implantation within the body of patients (claimed) during the treatment of restenosis.

ADVANTAGE - The polymeric coating containing therapeutic drugs provides controlled release of the drug in the localized environment, and contributes to great versatility of the vascular devices. The modular stents provide radially expanding force or support to a luminal structure; exhibit improved flexibility; and have decreased potential to module compaction.

Dwg.0/10
TECH UPTX: 20040728
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Component: At least one of (F1), (S1), and (P1) includes at least one therapeutic agent selected from anti-thrombotic agent, platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-beta), heparin, anti-inflammatory agent, anti-proliferation agent, rapamycin, angiopeptin, methotrexate, paclitaxel, anti-microbial agent, anti-metabolic agent, anti-platelet agent, anti-coagulant agent, Nitric Oxide releasing agent, **chaperone** inhibitor, benzoquinone ansamycins (e.g. geldanamycin, herbimycin and macbecin), glitazone, matrix metalloproteinase inhibitor (MMPI), antisense polynucleotide, transforming nucleotide, epothilones,

aspirin, **coumadin**, D-phenylalanyl-prolyl-arginine chloromethylketone (PPACK), hirudin, polypeptide from angiostatin and endostatin, 5-fluorouracil, estradiol, P-selectin glycoprotein ligand-1 chimera, abciximab, exochelin, eleutherobin and sarcodictyin, fludarabine, sirolimus, ABT-578, certican, Sulindac, tranilast, thiazolidiones (e.g. rosiglitazone, troglitazone, pioglitazone, darglitazone and englitazone), tetracycline, VEGF, insulin-like growth factor (IGF), fibroblast growth factor (FGF), Arg-Gly-Asp peptide, estrogen (e.g. 17 betaeta-estradiol), beta or gamma ray emitter (radioactive) agents, vasodilators (e.g. nitric oxide), various making agents (e.g. radio-opaque and/or echogenic materials).
Preferred Method: (M1) Further involves coating surfaces of (F1) and (S1) with the polymer material to form (P1), particularly applying the polymer material to (S1) and (F1) at a location where they contact each other. (P1) Is applied by dipping, spraying, and/or vapor deposition. (M1) further involves applying at least one therapeutic agent to at least one of (F1), (S1) and (P1).

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Component: At least one of (F1) and (S1) is manufactured from at least one material selected from stainless steel, tantalum, titanium, Nickel-Titanium alloy, shape memory alloy, super elastic alloy, low-modulus Ti-Nb-Zr alloy, and cobalt-nickel alloy steel (MP-35N). (F1) And (S1) are porous or non-porous.

TECHNOLOGY FOCUS - POLYMERS - Preferred Device: (P1) Comprises a polymer material applied to at least one surface of (F1) and (S1). (P1) Is applied to (S1) at a point of contact with (F1). (P1) Further comprises a polymer hinge that forms a gap between (F1) and (S1); and a polymer weld coupling (S1) to (F1) so that (S1) is in contact with (F1).
Preferred Components: (P1) Is manufactured from a biocompatible and biodegradable polymer selected from poly(L-lactic acid), polycaprolactone, poly(lactide-co-glycolide), poly(ethylene-vinyl acetate), poly(hydroxybutyrate-co-valerate), polydioxanone, polyorthoester, polyanhydride, poly(glycolic acid), poly(D,L-lactic acid), poly(glycolic acid-co-trimethylene carbonate), polyphosphoester, polyphosphoester urethane, poly(amino acids), cyanoacrylate, poly(trimethylene carbonate), poly(iminocarbonate), copoly(ether-ester), polyalkylene oxalate, polyphosphazene, biomolecule, fibrin, fibrinogen, cellulose, starch, collagen, hyaluronic acid, polyurethane, silicone, polyester, polyolefin, polyisobutytene, ethylene-alpha-olefin copolymer, acrylic polymer, acrylic copolymer, ethylene-co-vinylacetate, polybutylmethacrylate, vinyl halide polymer, vinyl halide copolymer, polyvinyl chloride, polyvinyl ether, polyvinyl methyl ether, polyvinylidene halide, polyvinylidene fluoride, polyvinylidene chloride, polyacrylonitrile, polyvinyl ketone, polyvinyl aromatic, polystyrene, polyvinyl ester, polyvinyl acetate, copolymer of vinyl monomer, ethylene-methyl methacrylate copolymer, acrylonitrile-styrene copolymer, ABS resin, ethylene-vinyl acetate copolymer, polyamide, Nylon 66, polycaprolactam, alkyl resin, polycarbonate, polyoxymethylene, polyimide, polyether, epoxy resin, polyurethane, rayon, rayon-triacetate, cellulose acetate/butyrate, cellophane, cellulose nitrate, cellulose propionate, cellulose ether, and carboxymethyl cellulose. At least one of (F1) and (S1) is manufactured from biocompatible polymers or biocompatible elastomer.

L102 ANSWER 2 OF 10 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-898528 [82] WPIX
DNC C2003-255363
TI New vaccine capable of modulating the immune system, useful for preventing or treating viral, bacterial or parasitic infections.
DC B04 B05 D16
IN BONAGURA, V R; DEVOTI, J; LANCE, H W; MAYHALL, J M; DEVOTI, J R
PA (BONA-I) BONAGURA V R; (DEVO-I) DEVOTI J; (LANC-I) LANCE H W; (MAYH-I) MAYHALL J M; (OMEG-N) OMEGA PHARM INC

CYC 102
PI US 2003175777 A1 20030918 (200382)* 52 A61K039-295
WO 2003074000 A2 20030912 (200382) EN A61K000-00
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW
AU 2003217877 A1 20030916 (200430) A61K039-295
ADT US 2003175777 A1 Provisional US 2002-354397P 20020204, Provisional US 2002-360788P 20020301, US 2003-357913 20030204; WO 2003074000 A2 WO 2003-US6430 20030303; AU 2003217877 A1 AU 2003-217877 20030303
FDT AU 2003217877 A1 Based on WO 2003074000
PRAI US 2003-357913 20030204; US 2002-354397P 20020204; US 2002-360788P 20020301
IC ICM A61K000-00; A61K039-295
ICS A01N043-04; A61K031-70; A61K039-116; C12Q001-68
AB US2003175777 A UPAB: 20031223
NOVELTY - A vaccine capable of modulating the immune system of a subject comprising a compound consisting of eleutheroside, coniferylaldehyde, caffeic acid ethyl ester, chlorogenic acid, sinapinalcohol, isofraxidin, syringaresinol or 6,8-dimethoxy-7-**hydroxycoumarin**, is new. The eleutheroside comprises a compound consisting of eleutheroside A, B, C, D, E, F or G.
ACTIVITY - Virucide; Antibacterial; Antiparasitic.
No biological data given.
MECHANISM OF ACTION - Vaccine.
USE - The vaccine is useful for modulating the immune system for preventing or treating viral, bacterial or parasitic infections (claimed).
Dwg.0/1
FS CPI
FA AB; DCN
MC CPI: B06-A01; B06-A02; B07-A02B; B10-C03; B10-D01; B14-A01; B14-A02; B14-B02; B14-S11; D05-H07
AB US2003175777 A UPAB: 20031223
NOVELTY - A vaccine capable of modulating the immune system of a subject comprising a compound consisting of eleutheroside, coniferylaldehyde, caffeic acid ethyl ester, chlorogenic acid, sinapinalcohol, isofraxidin, syringaresinol or 6,8-dimethoxy-7-**hydroxycoumarin**, is new. The eleutheroside comprises a compound consisting of eleutheroside A, B, C, D, E, F or G.
ACTIVITY - Virucide; Antibacterial; Antiparasitic.
No biological data given.
MECHANISM OF ACTION - Vaccine.
USE - The vaccine is useful for modulating the immune system for preventing or treating viral, bacterial or parasitic infections (claimed).
Dwg.0/1
TECH UPTX: 20031223
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Vaccine: The vaccine is capable of modulating the immune system of a subject. The modulation prevents or treats viral infections caused by e.g. HIV, hepatitis A, B, C or D virus, Dengue virus or Respiratory Syncytial virus, bacterial infections caused by e.g. Mycobacterium, Bacillus, Hemophilus, Pneumococcus or Streptococcus species, or parasitic infections caused by e.g. Plasmodium, Schistosoma or Leishmania species. The vaccine increases or decreases the expression of the protein, comprising interleukin (IL)-10, **heat shock protein** (**HSP**)-70b, **HSP**-70-2, **HSP**-40, **HSP-90**, heat shock transcription factor-4, c-Fos, junB, ATF-3, tumor necrosis factor (TNF)-alpha, human lymphoid transcription factor, CD14 differentiation antigen, Lck, platelet derived endothelial growth factor,

CCR2, CCR2a, CCR5 or CCR6.

ABEX UPTX: 20031223

ADMINISTRATION - The composition is administered via oral or parenteral route. No dosage given.

EXAMPLE - No relevant examples given.

L102 ANSWER 3 OF 10 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-229528 [22] WPIX
DNC C2003-059073
TI Synthesis and function inhibitors for **heat shock proteins** comprise vitamin K analog or **coumarin** anticoagulant derivatives.
DC B05
IN KAI, H
PA (KAIH-I) KAI H; (YAMA-I) YAMATSU T; (YAMA-I) YAMATSU I
CYC 100
PI WO 2003007927 A1 20030130 (200322)* JA 34 A61K031-122
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
JP 2003089636 A 20030328 (200331) 11 A61K031-122
ADT WO 2003007927 A1 WO 2002-JP6796 20020704; JP 2003089636 A JP 2002-8258 20020117
PRAI JP 2002-8258 20020117; JP 2001-212354 20010712
IC ICM A61K031-122
ICS A61K031-352; A61K031-37; A61P017-02; A61P025-28; A61P035-00; A61P043-00
ICA C07D311-56
AB WO2003007927 A UPAB: 20030402
NOVELTY - Synthesis and function inhibitors for **heat shock proteins** comprise a vitamin K analog or derivative or a **coumarin** anticoagulant or its derivative.
ACTIVITY - Cytostatic; Neuroprotective.
In assays using nude mice implanted with A549 cells administration of vitamin K2 at 50 mg/kg intraabdominally reduced tumor volume after 1 week compared to an increase in tumor volume in the control.
MECHANISM OF ACTION - HSP-Antagonist.
USE - As synthesis and function inhibitors for **heat shock proteins** for treating and preventing cancer and multiple sclerosis.
Dwg.0/10
FS CPI
FA AB; DCN
MC CPI: B04-N04; B14-F04
AB WO2003007927 A UPAB: 20030402
NOVELTY - Synthesis and function inhibitors for **heat shock proteins** comprise a vitamin K analog or derivative or a **coumarin** anticoagulant or its derivative.
ACTIVITY - Cytostatic; Neuroprotective.
In assays using nude mice implanted with A549 cells administration of vitamin K2 at 50 mg/kg intraabdominally reduced tumor volume after 1 week compared to an increase in tumor volume in the control.
MECHANISM OF ACTION - HSP-Antagonist.
USE - As synthesis and function inhibitors for **heat shock proteins** for treating and preventing cancer and multiple sclerosis.
Dwg.0/10
TECH UPTX: 20030402
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: **Heat**

shock protein has a molecular weight of 40-73 kD and **coumarin** anticoagulant or its derivative is **warfarin** or **dicumarol** or their salts.

ABEX UPTX: 20030402

ADMINISTRATION - Dosage is 0.01-50 (preferably 0.2-10) mg/kg orally or 0.002-10 (preferably 0.04-2) mg/kg parenterally.

L102 ANSWER 4 OF 10 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-140320 [13] WPIX
DNN N2003-111531 DNC C2003-035542
TI Use of a compound that e.g. inhibits **heat shock protein 90**, for treating disease associated with protein aggregation and amyloid formation e.g. polyglutamine expansion or Creutzfeld Jakob disease.
DC B05 S03
IN HARTL, U; SITTLER, A; WANKER, E
PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN
CYC 101
PI WO 2002094259 A1 20021128 (200313)* EN 23 A61K031-395
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
EP 1387678 A1 20040211 (200411) EN A61K031-395
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2002094259 A1 WO 2002-EP4893 20020503; EP 1387678 A1 EP 2002-740561 20020503, WO 2002-EP4893 20020503
FDT EP 1387678 A1 Based on WO 2002094259
PRAI US 2001-288718P 20010504; EP 2001-110769 20010503
IC ICM A61K031-395
ICS A61K031-365; A61P025-28; G01N033-566
AB WO 200294259 A UPAB: 20030224
NOVELTY - Use of a compound(s) that inhibit **heat shock protein** (**Hsp**) **90**, binding to HSF1 to **Hsp90** or that activate expression of both Hsp40 and Hsp70 for treating or preventing disease associated with protein aggregation and amyloid formation.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) Designing a drug for the treatment of disease associated with protein aggregation and amyloid formation involving:

(a) identifying the sites of compound that binds Hsp40 and/or 70 or identifying sites of a compound that binds to **Hsp 90** or to HSF-1 and/or their homologues or other components participating in the regulation of the stress protein response,

(b) molecular modeling of both the binding sites in the compound and the Hsp, and

(c) modifying the compound to improve its binding specificity for the Hsp or HSF-1;

(2) Identifying an activator of the expression of Hsp40 and/or 70 involving testing small molecules or peptides for the activation of translation, or testing a compound for the activation of transcription. The compound binds to the promoter region of the genes encoding the Hsp and preferably with transcription factors and their responsive elements;

(3) Identifying an inhibitor of **Hsp90** involving testing a compound selected from small molecules or peptides for inhibition of **Hsp90** ATPase activity function, and selecting a compound that tests positive;

(4) Identifying an inhibitor of binding of HSF-1 to **Hsp90**

involving testing a compound for inhibition of binding of HSF-1 to **Hsp90**, and selecting a compound that tests positive.

ACTIVITY - Neuroprotective; Nootropic; Anticonvulsant; Antidiabetic; Antiparkinsonian.

MECHANISM OF ACTION - **Hsp 90** inhibitor; Inhibitor of binding to HSF1 to **Hsp90**; Activator of expression of both Hsp40 and Hsp70.

In order to induce a heat shock response COS-1 cells expressing the fusion of enhanced green fluorescent protein (EGFP) and the huntingtin exon 1 protein with 72 glutamines (HD72Q) were treated with various concentrations of geldamycine (GA). Forty hours post transfection, total cell extracts were prepared and expression of EGFP-HD72Q protein migrating in the SDS-gel at approx. 57 kDa was detected in protein extracts of untransfected control cells. Treatment of cells with increasing concentration of GA (18-360 nM) had no effect on EGFP-HD72Q expression. In contrast, the expression of each of the molecular **chaperones** **Hsp**-40, **Hsp**-70 and **Hsp-90** increased with increasing GA-concentrations, indicating that treatment of cells with GA triggers heat shock response. Addition of GA to final concentration of 360 nM resulted in 3-4 fold up-regulation of Hsp40, Hsp70 and **Hsp90** compared to the untreated control.

USE - The compounds are used for treating or preventing disease associated with protein aggregation and amyloid formation such as polyglutamine expansion; for treating Creutzfeld Jakob disease, Huntington's disease, spinal and bulbar muscular atrophy, dentarorubral pallidoluysian atrophy, spinocerebellar ataxia type 1, 2, 3, 6 or 7, Alzheimer disease, primary systemic amyloidosis, secondary systemic amyloidosis, senile systemic amyloidosis, familial amyloid polyneuropathy I, hereditary cerebral amyloid angiopathy, hemodialysis-related amyloidosis, familial amyloid polyneuropathy III, Finnish hereditary systemic amyloidosis, type II diabetes, medullary carcinoma of the thyroid, spongiform encephalopathies: Kuru, Gerstmann-Straussler-Scheinker syndrome (GSS), familial insomnia, scrapie, atrial amyloidosis, hereditary non-neuropathic systemic amyloidosis, injection-localized amyloidosis, hereditary renal amyloidosis and Parkinson's disease.

ADVANTAGE - The compound modifies site of action, spectrum of activity, improves organ specificity and potency. It also decreases toxicity and side effects, whilst modifying onset of therapeutic action, duration of effect, pharmacokinetic parameters (resorption, distribution, metabolism and excretion), and physico-chemical parameters (solubility, hygroscopicity, color, taste, odor, stability, state).

Dwg.0/6

FS CPI EPI

FA AB; DCN

MC CPI: B04-C01; B04-E01; B04-H01; B04-L01; B04-N04; B06-H; B11-C08E; B11-C08F3; B11-C08F4; B12-K04E; B14-J01A3; B14-J01A4; B14-J01B4; B14-N10; B14-N11; B14-N16; B14-S04

EPI: S03-E14H4

AB WO 200294259 A UPAB: 20030224

NOVELTY - Use of a compound(s) that inhibit **heat shock protein** (**Hsp**) **90**, binding to HSF1 to **Hsp90** or that activate expression of both Hsp40 and Hsp70 for treating or preventing disease associated with protein aggregation and amyloid formation.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) Designing a drug for the treatment of disease associated with protein aggregation and amyloid formation involving:

(a) identifying the sites of compound that binds Hsp40 and/or 70 or identifying sites of a compound that binds to **Hsp 90** or to HSF-1 and/or their homologues or other components participating in the regulation of the stress protein response,

(b) molecular modeling of both the binding sites in the compound and

the Hsp, and

(c) modifying the compound to improve its binding specificity for the Hsp or HSF-1;

(2) Identifying an activator of the expression of Hsp40 and/or 70 involving testing small molecules or peptides for the activation of translation, or testing a compound for the activation of transcription. The compound binds to the promoter region of the genes encoding the Hsp and preferably with transcription factors and their responsive elements;

(3) Identifying an inhibitor of **Hsp90** involving testing a compound selected from small molecules or peptides for inhibition of **Hsp90** ATPase activity function, and selecting a compound that tests positive;

(4) Identifying an inhibitor of binding of HSF-1 to **Hsp90** involving testing a compound for inhibition of binding of HSF-1 to **Hsp90**, and selecting a compound that tests positive.

ACTIVITY - Neuroprotective; Nootropic; Anticonvulsant; Antidiabetic; Antiparkinsonian.

MECHANISM OF ACTION - **Hsp 90** inhibitor; Inhibitor of binding to HSF1 to **Hsp90**; Activator of expression of both Hsp40 and Hsp70.

In order to induce a heat shock response COS-1 cells expressing the fusion of enhanced green fluorescent protein (EGFP) and the huntingtin exon 1 protein with 72 glutamines (HD72Q) were treated with various concentrations of geldamycine (GA). Forty hours post transfection, total cell extracts were prepared and expression of EGFP-HD72Q protein migrating in the SDS-gel at approx. 57 kDa was detected in protein extracts of untransfected control cells. Treatment of cells with increasing concentration of GA (18-360 nM) had no effect on EGFP-HD72Q expression. In contrast, the expression of each of the molecular **chaperones** **Hsp**-40, **Hsp**-70 and **Hsp-90** increased with increasing GA-concentrations, indicating that treatment of cells with GA triggers heat shock response. Addition of GA to final concentration of 360 nM resulted in 3-4 fold up-regulation of Hsp40, Hsp70 and **Hsp90** compared to the untreated control.

USE - The compounds are used for treating or preventing disease associated with protein aggregation and amyloid formation such as polyglutamine expansion; for treating Creutzfeld Jakob disease, Huntington's disease, spinal and bulbar muscular atrophy, dentarorubral pallidoluysian atrophy, spinocerebellar ataxia type 1, 2, 3, 6 or 7, Alzheimer disease, primary systemic amyloidosis, secondary systemic amyloidosis, senile systemic amyloidosis, familial amyloid polyneuropathy I, hereditary cerebral amyloid angiopathy, hemodialysis-related amyloidosis, familial amyloid polyneuropathy III, Finnish hereditary systemic amyloidosis, type II diabetes, medullary carcinoma of the thyroid, spongiform encephalopathies: Kuru, Gerstmann-Straussler-Scheinker syndrome (GSS), familial insomnia, scrapie, atrial amyloidosis, hereditary non-neuropathic systemic amyloidosis, injection-localized amyloidosis, hereditary renal amyloidosis and Parkinson's disease.

ADVANTAGE - The compound modifies site of action, spectrum of activity, improves organ specificity and potency. It also decreases toxicity and side effects, whilst modifying onset of therapeutic action, duration of effect, pharmacokinetic parameters (resorption, distribution, metabolism and excretion), and physico-chemical parameters (solubility, hygroscopicity, color, taste, odor, stability, state).

Dwg.0/6

TECH UPTX: 20030224

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Method: Identification is effected by site-directed mutagenesis and/or chimeric protein studies. The compound is derived from geldamycin by modeling geldamycin by peptidomimetic and chemically synthesizing the modeled compound. The compound can also be obtained by screening at least partially randomized peptide library and/or chemical compounds library for the compound. The modification is achieved by either:

(1) Esterification of carboxyl groups;
(2) Esterification of hydroxyl groups with carbon acids;
(3) Esterification of hydroxyl groups to, e.g. phosphates, pyrophosphates or sulfates or hemi succinates;
(4) Formation of salts or complexes;
(5) Synthesis of pharmacologically active polymers;
(6) Introduction of hydrophilic moieties;
(7) Introduction/exchange of substituents on aromates or side chains, change of substituent pattern;
(8) Modification by introduction of isosteric or bioisosteric moieties;
(9) Synthesis of homologous compounds;
(10) Introduction of branched side chains;
(11) Conversion of alkyl substituents to cyclic analogues;
(12) Derivatization of hydroxyl group to ketals, acetals;
(13) N-acetylation to amides, phenylcarbamates;
(14) Synthesis of Mannich bases, imines; and/or
(15) Transformation of ketones or aldehydes to Schiff's bases, oximes, acetals, ketals, enolesters, oxazolidines, thiozolidines.
Inhibition or activation of the **heat shock protein** is assayed by Reporter assays, immunofluorescence microscopy, a filter retardation assay or ATPase assays.

TECHNOLOGY FOCUS - BIOLOGY - Preferred Protein: The Hsp is human **heat shock protein.** The Hsp40 is Hdj-1 or Hdj-2.

ABEX UPTX: 20030224
SPECIFIC COMPOUNDS - The use of Geldanamycin, Radicicol, Herbimycin A, **Novobiocin**, 17-allylamino-17-demethoxygeldanamycin and macbecin are specifically claimed as the compound.

ADMINISTRATION - The compound is administered intravenously, intraperitoneally, subcutaneously, intramuscularly, topically, intradermally, intranasally or intrabroncheally. The dosage is 0.001-1000 microg or 1 microg -10 mg units/per kg body weight per minutes for continuous infusion.

L102 ANSWER 5 OF 10 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-147972 [19] WPIX
DNC C2002-045967
TI Use of collagen promoter such as geldanamycin, for treating fibrogaic disorder.
DC B02
IN STREHLOW, D
PA (UYBO-N) UNIV BOSTON; (STRE-I) STREHLOW D
CYC 95
PI WO 2002002123 A1 20020110 (200219)* EN 51 A61K031-66
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001071567 A 20020114 (200237) A61K031-66
US 2004082498 A1 20040429 (200429) A61K031-00
ADT WO 2002002123 A1 WO 2001-US20578 20010628; AU 2001071567 A AU 2001-71567 20010628; US 2004082498 A1 WO 2001-US20578 20010628, US 2002-312287 20021220
FDT AU 2001071567 A Based on WO 2002002123
PRAI US 2000-214950P 20000629; US 2002-312287 20021220
IC ICM A61K031-00; A61K031-66
ICS A61K031-70; A61K039-395
AB WO 200202123 A UPAB: 20020321
NOVELTY - A composition (A) comprises an inhibitor of a collagen promoter

(preferably an inhibitor of **heat shock protein 90** alpha (HSO **90**) **chaperone** function) and an inert carrier vehicle for topical application.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for an article comprising a packaging material and (A). The packaging material also comprises a label with instructions for use.

ACTIVITY - Dermatological; Immunosuppressive; Antirheumatic; Antarthritic; Hepatoprotic; Anti-inflammatory; Ophthalmological.

No biological data given.

MECHANISM OF ACTION - Collagen promoter inhibitor (preferably **Hsp 90 chaperone** inhibitor); TGF- beta signal transduction blocker; Smad-controlled promoter activation inhibitor.

USE - For prophylaxis or treatment of a fibrogenic disorder e.g. scleroderma, polymyositis, systemic lupus erythematosis, rheumatoid arthritis, keloid formulation, formulation, interstitial nephritis and pulmonary fibrosis or liver cirrhosis (all claimed).

ADVANTAGE - The composition does not detectably affect steroid hormone receptor activity; decreases Smad DNA binding and has no effect on the PN1 promoter.

Dwg.0/11

FS CPI

FA AB; DCN

MC CPI: B02-Z; B06-H; B14-C09B; B14-G02D; B14-K01; B14-N10; B14-N12

AB WO 200202123 A UPAB: 20020321

NOVELTY - A composition (A) comprises an inhibitor of a collagen promoter (preferably an inhibitor of **heat shock protein 90** alpha (HSO **90**) **chaperone** function) and an inert carrier vehicle for topical application.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for an article comprising a packaging material and (A). The packaging material also comprises a label with instructions for use.

ACTIVITY - Dermatological; Immunosuppressive; Antirheumatic; Antarthritic; Hepatoprotic; Anti-inflammatory; Ophthalmological.

No biological data given.

MECHANISM OF ACTION - Collagen promoter inhibitor (preferably **Hsp 90 chaperone** inhibitor); TGF- beta signal transduction blocker; Smad-controlled promoter activation inhibitor.

USE - For prophylaxis or treatment of a fibrogenic disorder e.g. scleroderma, polymyositis, systemic lupus erythematosis, rheumatoid arthritis, keloid formulation, formulation, interstitial nephritis and pulmonary fibrosis or liver cirrhosis (all claimed).

ADVANTAGE - The composition does not detectably affect steroid hormone receptor activity; decreases Smad DNA binding and has no effect on the PN1 promoter.

Dwg.0/11

TECH UPTX: 20020321

TECHNOLOGY FOCUS - BIOLOGY - Preferred Components: Geldanamycin, macbecin I and II, herbimycin, radiciol and **novobiocin** are claimed as the inhibitor of **Hsp 90-chaperone** function.

ABEX UPTX: 20020321

ADMINISTRATION - The composition is administered locally (preferably topically), orally or parenterally (including intranasally, subcutaneously, intramuscularly, intravenously or intra-arterially) in dosage of 0.05 - 10 (preferably 0.25 - 2.5) microg/kg/day. For a 70 kg human patient the dosage is 50 mug/day.

EXAMPLE - None given.

L102 ANSWER 6 OF 10 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2001-542488 [61] WPIX

DNC C2001-162030

TI Medicament for inducing tolerance to antigens, e.g. those causing autoimmune disease, allergy or infections, containing the antigen together with steroid sulfatase inhibitor as adjuvant to improve tolerance

induction.
DC B04 B05 D16
IN WICKENS, T
PA (BION-N) BIONETWORKS GMBH
CYC 1
PI DE 10005643 A1 20010816 (200161)* 9 A61K039-39
ADT DE 10005643 A1 DE 2000-10005643 20000209
PRAI DE 2000-10005643 20000209
IC ICM A61K039-39
AB DE 10005643 A UPAB: 20011024
NOVELTY - A medicament (A) contains as active component a combination of a steroid sulfatase (SS) inhibitor (I) and an antigen (II).
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a composition comprising (I) and (II).
ACTIVITY - Immunosuppressive; antiallergic; antirheumatic; antiarthritic; neuroprotective; ophthalmological; antiinflammatory; antidiabetic; dermatological; antibacterial; virucidal; antifungal; antitubercular.
In tolerance tests involving experimental autoimmune encephalitis in rats (an animal model of multiple sclerosis), administration of SS inhibitors (e.g. 1-8 mg of estrone-3-O-sulfamate (Ia) in oil, subcutaneously) before sensitization markedly reduced the amount of antigen (i.e. MBP or MOG) required to produce tolerance (no quantitative results given).
MECHANISM OF ACTION - Steroid sulfatase inhibitor; vaccine.
USE - (A) is used for induction of tolerance (especially mucosal tolerance) (claimed). The claims also cover the use of (I) in combination with (II) for induction of tolerance; and a method for inducing tolerance in the control of autoimmune diseases, allergies, transplant rejection and graft-versus-host-disease in humans or other mammals, involving administration of (I) in combination with the administration of (II) (or a nucleic acid encoding (II)). (II) include antigens associated with rheumatoid arthritis, multiple sclerosis, uveitis, type I diabetes, lupus erythematosus or infectious diseases; benzoyl penicillin, insulin, ovalbumin or lactalbumin; and components of pollen, foods or house dust mites (all claimed). Infection-associated (II) include bacterial, viral or fungal antigens, such as influenza, leishmania, cytomegalovirus, pneumonia, Streptococcus B, Chlamydia, Helicobacteria, hepatitis C, human papilloma virus or Mycobacterium tuberculosis antigens.
ADVANTAGE - Combining (I) (as adjuvant) with (II) improves and optimizes the induction of tolerance to a wide range of (II). In particular the combination of (I) and (II) provides an effective, well tolerated oral vaccine.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B01-A01; B02-P; B04-C02; B04-C02V; B04-D01; B04-E01; B04-E02A; B04-E03A; B04-E06; B04-F01; B04-F10; B04-F10B4; B04-F11; B04-J03A; B04-N02; B04-N04; B04-N06; B06-A01; B10-A08; B14-A01; B14-A01B1; B14-A01B2; B14-A02; B14-A02A3; B14-A02A6; B14-A02B2; B14-A03; B14-A04; B14-C09B; B14-G02A; B14-G02C; B14-G02D; B14-N03; B14-N12; B14-N17; B14-S01; B14-S04; B14-S11; D05-H07; D05-H12A; D05-H12D2; D05-H17A6
AB DE 10005643 A UPAB: 20011024
NOVELTY - A medicament (A) contains as active component a combination of a steroid sulfatase (SS) inhibitor (I) and an antigen (II).
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a composition comprising (I) and (II).
ACTIVITY - Immunosuppressive; antiallergic; antirheumatic; antiarthritic; neuroprotective; ophthalmological; antiinflammatory; antidiabetic; dermatological; antibacterial; virucidal; antifungal; antitubercular.
In tolerance tests involving experimental autoimmune encephalitis in

rats (an animal model of multiple sclerosis), administration of SS inhibitors (e.g. 1-8 mg of estrone-3-O-sulfamate (Ia) in oil, subcutaneously) before sensitization markedly reduced the amount of antigen (i.e. MBP or MOG) required to produce tolerance (no quantitative results given).

MECHANISM OF ACTION - Steroid sulfatase inhibitor; vaccine.

USE - (A) is used for induction of tolerance (especially mucosal tolerance) (claimed). The claims also cover the use of (I) in combination with (II) for induction of tolerance; and a method for inducing tolerance in the control of autoimmune diseases, allergies, transplant rejection and graft-versus-host-disease in humans or other mammals, involving administration of (I) in combination with the administration of (II) (or a nucleic acid encoding (II)). (II) include antigens associated with rheumatoid arthritis, multiple sclerosis, uveitis, type I diabetes, lupus erythematosus or infectious diseases; benzoyl penicillin, insulin, ovalbumin or lactalbumin; and components of pollen, foods or house dust mites (all claimed). Infection-associated (II) include bacterial, viral or fungal antigens, such as influenza, leishmania, cytomegalovirus, pneumonia, Streptococcus B, Chlamydia, Helicobacteria, hepatitis C, human papilloma virus or Mycobacterium tuberculosis antigens.

ADVANTAGE - Combining (I) (as adjuvant) with (II) improves and optimizes the induction of tolerance to a wide range of (II). In particular the combination of (I) and (II) provides an effective, well tolerated oral vaccine.

Dwg.0/0

TECH UPTX: 20011024

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred SS Inhibitors: (I) are selected from endogenous or exogenous SS inhibitors and antisense nucleic acids, including specific inhibitors for one or more SS isoenzymes. (I) is especially selected from compound having sulfamate groups bonded to an aryl ring (specifically estrone sulfamates, p-(O-sulfamoyl)-N-alkanoyl-tyramines or **coumarin** sulfamates) and flavonoids or their derivatives.

Preferred Antigens: (II) are selected from natural or synthetic proteins, peptides, nucleic acids, altered peptide ligands, carbohydrates (including polysaccharides), lipopolysaccharides and antigens from biological resources (specifically bystander antigens); antigens associated with rheumatoid arthritis, multiple sclerosis, uveitis, type I diabetes, lupus erythematosus or infectious diseases; **heat-shock proteins**, proteolipids, myelin basic protein (MBP), myelin oligodendrocyte glycoprotein (MOG) or cell components of the uvea, skin, epithelium, thyroid, basal membrane, muscles, nerve cells, thymus or erythrocytes (of endogenous or other origin); or benzoyl penicillin, insulin, ovalbumin, lactalbumin or components of pollen, foods or house dust mites. (II) may be used in the form of a nucleic acid encoding the antigen.

Preferred Composition: (I) and (II) may be present separately. (A) may additionally contain auxiliaries, additives and/or adjuvants.

ABEX UPTX: 20011024

SPECIFIC COMPOUNDS - Use of 25 compounds (I) is disclosed, e.g. estrone-3-O-sulfamate (Ia), p-O-sulfamoyl-N-tetradecanoyl-tyramine, 4-methyl-**coumarin**-7-O-sulfamate and dadzein-4'-O-sulfate.

ADMINISTRATION - Daily dose of (I) is 0.01-100 (preferably 1-10) mg/kg; and the weight ratio of (I) to (II) is 0.1-99.99 : 99.9-0.01 (preferably 10-90 : 90-10). (I) and (II) may be administered together or separately, e.g. by oral, intranasal, inhalation or parenteral routes.

L102 ANSWER 7 OF 10 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-281566 [29] WPIX
DNC C2001-085553
TI New amide compounds with antibacterial activity against Gram negative bacteria, and new fluorinated linker compounds useful in their

preparation.
DC B05 B06
IN FEX, T; HULTGREN, S J; KIHLBERG, J; LARSSON, A; PINKNER, J; SVENSSON, A
PA (UNIW) UNIV WASHINGTON
CYC 94
PI WO 2001020995 A1 20010329 (200129)* EN 85 A01N057-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000078320 A 20010424 (200141) A01N057-00
ADT WO 2001020995 A1 WO 2000-US26177 20000922; AU 2000078320 A AU 2000-78320 20000922
FDT AU 2000078320 A Based on WO 2001020995
PRAI US 1999-155822P 19990923
IC ICM A01N057-00
ICS C07D305-00; C07D309-00; C07D311-00; C07D311-02; C07D311-04; C07D321-00
AB WO 200120995 A UPAB: 20010528
NOVELTY - Amide derivatives (I) inhibit growth of Gram-negative bacteria by inhibiting or preventing pilus biogenesis.
DETAILED DESCRIPTION - Amide derivatives of formula (I), and their salts, esters or amines, are new:
R1, R2, R3 = 1 10C alkyl, 2-15C acyl, 6-14C aryl, heteroaryl, 7-15C arylalkyl, heteroarylalkyl or heterocycloalkyl, each optionally substituted;
R4 = CO2H, CONH2, -CHO, -B(OH)2, -PO(OH)2 or -COR; and
R = 13C alkyl optionally halo-substituted.
INDEPENDENT CLAIMS are included for the following:
(a) preparation and uses of (I);
(b) a new linker compound of formula (II):
(c) preparation of (II);
(d) a library of compounds (I);
(e) a method for monitoring solid-phase synthesis of (I) using a linker compound attached to a solid support; and
(f) a complex comprising (I) complexed with a linker compound fixed to a solid support.
R'1 = CO2H, -(CH2)nCO2H or O(CH2)nCO2H;
n = 1-10; and
R'2, R'3 = F or H, provided that when either R'2 or R'3 is F, then the other is H.
ACTIVITY - Antibacterial.
MECHANISM OF ACTION - Pili assembly inhibitor.
(I) bind to a pilus **chaperone** (PapD **chaperone** or FimC **chaperone**) inhibiting pili assembly. In a test to determine inhibition of formation of the complex between PapD and PapG, % inhibition of the complex between PapD and PapG at an inhibitor/PapD ratio of 38, was 31.5 % for N-benzyl-N-(2-oxo-2H-1-benzopyran-3-carbonyl) glycine.
USE - For treating, preventing or inhibiting bacterial infections caused by Gram-negative organisms e.g. Escherichia coli, Haemophilus influenzae, Salmonella enteriditis, Salmonella typhimurium, Bordetella pertussis, Yersinia pestis, Yersinia enterocolitica, Helicobacter pylori and Klebsiella pneumoniae, and preventing or inhibiting biofilm formation or bacterial colonization by a Gram negative organism. (I) may be administered alone or in combination with other antibiotics.
Dwg.0/4
FS CPI
FA AB; GI; DCN
MC CPI: B10-C04B; B10-D03; B11-C08; B12-K04A; B14-A01A
AB WO 200120995 A UPAB: 20010528
NOVELTY - Amide derivatives (I) inhibit growth of Gram-negative bacteria

by inhibiting or preventing pilus biogenesis.

DETAILED DESCRIPTION - Amide derivatives of formula (I), and their salts, esters or amines, are new:

R1, R2, R3 = 1 10C alkyl, 2-15C acyl, 6-14C aryl, heteroaryl, 7-15C arylalkyl, heteroarylalkyl or heterocycloalkyl, each optionally substituted;

R4 = CO2H, CONH2, -CHO, -B(OH)2, -PO(OH)2 or -COR; and

R = 13C alkyl optionally halo-substituted.

INDEPENDENT CLAIMS are included for the following:

(a) preparation and uses of (I);

(b) a new linker compound of formula (II):

(c) preparation of (II);

(d) a library of compounds (I);

(e) a method for monitoring solid-phase synthesis of (I) using a linker compound attached to a solid support; and

(f) a complex comprising (I) complexed with a linker compound fixed to a solid support.

R'1 = CO2H, -(CH2)nCO2H or O(CH2)nCO2H; n = 1-10; and

R'2, R'3 = F or H, provided that when either R'2 or R'3 is F, then the other is H.

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - Pili assembly inhibitor.

(I) bind to a pilus **chaperone** (PapD **chaperone** or FimC **chaperone**) inhibiting pili assembly. In a test to determine inhibition of formation of the complex between PapD and PapG, % inhibition of the complex between PapD and PapG at an inhibitor/PapD ratio of 38, was 31.5 % for N-benzyl-N-(2-oxo-2H-1-benzopyran-3-carbonyl) glycine.

USE - For treating, preventing or inhibiting bacterial infections caused by Gram-negative organisms e.g. Escherichia coli, Haemophilus influenzae, Salmonella enteriditis, Salmonella typhimurium, Bordetella pertussis, Yersinia pestis, Yersinia enterocolitica, Helicobacter pylori and Klebsiella pneumoniae, and preventing or inhibiting biofilm formation or bacterial colonization by a Gram negative organism. (I) may be administered alone or in combination with other antibiotics.

Dwg.0/4

TECH UPTX: 20010528

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation of Linker: Preparation of the linker compounds comprises:

(a) hydrolyzing 1 of the ester moieties of dimethyl-2-fluoroterephthalate;

(b) reducing the remaining ester; and

(c) separating the 2 regioisomers.

Alternatively, the linker compounds are produced by:

(a) dealkylating a 2-fluoro-4-propoxybenzoic acid;

(b) reducing the carboxylic acid group to give a hydroxymethylphenol compound;

(c) alkylating the phenolic hydroxyl group; and

(d) hydrolyzing the product from (c) under basic conditions.

Preparation of (I): (I) can be prepared by:

(1) condensing a compound of formula (III) with a salicylaldehyde, followed by cleavage from the solid support, to give a compound of formula (IA), i.e. (I) where R1 = H; R2 = (CH2)mA (m = 0-3; A = n-butyl, 2-methoxyethyl, benzyl or 2-(3-indolyl)-ethyl); R3 = **coumarin**; R4 = carboxyl; or

(2) the following steps:

(i) affixing a linker compound onto a solid support to give a benzylic alcohol;

(ii) subjecting the benzylic alcohol to acylation with bromoacetic acid;

(iii) subjecting the bromoacetate to a nucleophilic substitution with an amine;

(iv) acylating with ethyl malonyl chloride to form an N-alkyl-N (malonamic acid ethyl ester)-glycine derivative;

(v) condensing the product from (iv) with a salicylaldehyde; and

(vi) cleaving the compound from the linker compound under acidic or basic conditions.
Solid phase synthesis of (I) can be monitored by affixing the linker compound onto a solid support (e.g. polystyrene resin beads, silica chips and polyethylene glycol resins); measuring a signal from the linker compound and using the signal as an internal reference to monitor reactions. Typically the signal originating from the linker compound is a 19F resonance, which is measured by NMR spectroscopy.

ABEX UPTX: 20010528
SPECIFIC COMPOUNDS - 8 Compounds (I) are specifically claimed, e.g. N-benzyl-N-(2-oxo-2H-1-benzopyran-3-carbonyl) glycine of formula (Ia); and N-(2-(1H-indol-3-yl)-ethyl)-N-(3-oxo-3H naphtho(2,1-b)pyran-2-carbonyl)-glycine. 4 Compounds (II) are specifically claimed, e.g. 3-fluoro-4 hydroxymethyl-phenoxy-acetic acid of formula (IIa):

ADMINISTRATION - Administration is by conventional routes.
Daily dosage is 1-1000 microg/kg.
EXAMPLE - N,N'-Diisopropylcarbodiimide (835 microl) was added to an ice-cold solution of pentafluorophenol (1.99 g) in EtOAc (30 ml). After 30 minutes, 3-fluoro-4-hydroxymethyl-phenoxyacetic acid (1.13 g) was added and the solution was stirred at 0 degrees C for 60 minutes. The mixture was added to resin (10 g), stirred for 12 hours at ambient temperature, washed and dried to give resin A.
DIC (1.04 ml) was added to a solution of bromoacetic acid (1.13 g) and 1-hydroxybenzotriazole (729 mg) in THF (30 ml), stirred and added to resin A (2.7 mmol, pre-swollen in THF), with N,N' dimethylaminopyridine (108 mg) in THF (10 ml). After stirring overnight, the resin was washed and dried.
A solution of benzylamine (3 equivalents) in MeCN (30 ml) was added to the resin (2.7 mmol) at 0 degrees C, and after stirring for 90 minutes, the mixture was washed and dried.
Ethyl malonyl chloride (1.02 ml) in CH2Cl2 (10 ml) was added to a suspension of the resin (2.7 mmol) and N,N'-diisopropylethylamine (1.38 ml) in CH2Cl2 (20 ml) at 0 degrees C. After stirring for 60 minutes at 0 degrees C, the resin was washed and dried. A solution of salicylaldehyde (3 equivalents) in MeCN (7 ml) was added to the resin (pre-swollen in MeCN). The mixture was refluxed, and piperidine (1.2 equivalents) in MeCN (1 ml) added. After refluxing overnight, the resin was cooled, washed and dried.
Aqueous LiOH (1 M, 5 ml) was added to the resin (0.54 mmol) in THF/H2O/MeOH (3:1:1, 40 ml) at 0 degrees C. After 2.5 hours at ambient temperature, the resin was filtered off. The filtrate concentrated almost to dryness, then concentrated from toluene. The residue was dissolved in a mixture of EtOAc (30 ml) and aqueous HCl (0.05 M, 10 ml). The organic phase was worked up and flash column chromatography gave N-benzyl-N-(2-oxo-2H-1 benzopyran-3-carbonyl)-glycine (44 %).

L102 ANSWER 8 OF 10 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2000-572228 [53] WPIX
DNC C2000-170660
TI Method of inhibiting binding of a **chaperone** protein, with its client protein or client polypeptide, using a **coumarin** or a **coumarin** derivative.
DC B02
IN MARCU, M G; NECKERS, L M; SCHULTE, T W
PA (USSH) US DEPT HEALTH & HUMAN SERVICES
CYC 92
PI WO 2000053169 A2 20000914 (200053)* EN 20 A61K031-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000037406 A 20000928 (200067)
EP 1161231 A2 20011212 (200204) EN A61K031-00
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2003523313 W 20030805 (200353) 30 A61K031-353
ADT WO 2000053169 A2 WO 2000-US6482 20000310; AU 2000037406 A AU 2000-37406 20000310; EP 1161231 A2 EP 2000-916277 20000310, WO 2000-US6482 20000310; JP 2003523313 W JP 2000-603658 20000310, WO 2000-US6482 20000310
FDT AU 2000037406 A Based on WO 2000053169; EP 1161231 A2 Based on WO 2000053169; JP 2003523313 W Based on WO 2000053169
PRAI US 1999-124135P 19990312
IC ICM A61K031-00; A61K031-353
ICS A61K031-7048; A61K031-7052; A61P031-20; A61P035-00; A61P043-00; C07D311-10; C07D311-46; C07D311-56; C07H017-075; C12N009-99
AB WO 200053169 A UPAB: 20001023
NOVELTY - A method of inhibiting binding of a **chaperone** protein, with its client protein or client polypeptide, using a **coumarin** or a **coumarin** derivative.

DETAILED DESCRIPTION - A method of inhibiting binding of a **chaperone** protein with its client protein or client polypeptide. The **chaperone** protein is contacted with a **coumarin** or a **coumarin** derivative, such that the **coumarin** or the **coumarin** derivative binds the **chaperone** protein, which inhibits the **chaperone** protein from binding its client protein or client polypeptide. The client protein or the client polypeptide is inactive or less active subsequent to binding of the **chaperone** protein to **coumarin** or the **coumarin** derivative.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - **Chaperone** protein antagonist.

To demonstrate binding of a **chaperone** protein to **novobiocin**, the **novobiocin** was first immobilized on sepharose. A **chaperone** protein, either pure **Hsp90**, or a solution containing **Hsp90** in a cell lysate, was subsequently incubated with the immobilized **novobiocin**. The cell lysate was preincubated with various members of the **coumarin** family of antibiotics, namely **novobiocin**, **chlorobiocin** or **coumermycin** A1 and also ATP to determine their ability to inhibit binding of the **Hsp90**. The amount of **Hsp90** bound to the imobilized **novobiocine** was analyzed. Imobilized **novobiocin** bound in a hydrophobic manner to both of the pure **Hsp90** and the **Hsp90** present in cell lysate. Pre-incubation of the cell lysate with excess soluble **novobiocin**, **chlorobiocin**, **coumermycin** A1, or ATP inhibited, in a dose-dependent manner, subsequent **Hsp90** binding to imobilized **novobiocin**. Soluble **novobiocin** inhibited **Hsp90** binding to imobilized **novobiocin** at 8 mM. **Chlorobiocin** and **coumermycin** A1 inhibited **Hsp90** binding to imobilized **novobiocin** at 0.5 mM, while ATP inhibited **Hsp90** binding between 10 and 15 mM, as demonstrated by silver staining.

These data demonstrate that **novobiocin** binds to **chaperone** proteins such as **Hsp90** and that subsequent **Hsp90**-binding can be inhibited by contact with the **coumarin** derivatives.

USE - Used as **chaperone** protein antagonist. **Chaperone** proteins interact with a variety of proteins involved in cell proliferation. One such **chaperone** protein, **heat shock protein** (**Hsp**)**90** is expressed at 2-10 fold higher levels in tumor cells compared to their normal counterparts (see Ferrarini et al., Int. J. Cancer 51:613-619 (1992)). Method can be used to interfere with the **chaperone** protein function of **Hsp90**. The **coumarin** or a **coumarin** derivative can be used to bind **Hsp90** and to interfere with its

function, including its function in tumor cell proliferation.

ADVANTAGE - Present method better suited in clinical applications compared to the use of other compounds of prior art which display in vivo toxicity unrelated to their **Hsp90** antagonism.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B02-C01; B02-N; B06-A01; B14-H01B; B14-L06

AB WO 200053169 A UPAB: 20001023

NOVELTY - A method of inhibiting binding of a **chaperone** protein, with its client protein or client polypeptide, using a **coumarin** or a **coumarin** derivative.

DETAILED DESCRIPTION - A method of inhibiting binding of a **chaperone** protein with its client protein or client polypeptide. The **chaperone** protein is contacted with a **coumarin** or a **coumarin** derivative, such that the **coumarin** or the **coumarin** derivative binds the **chaperone** protein, which inhibits the **chaperone** protein from binding its client protein or client polypeptide. The client protein or the client polypeptide is inactive or less active subsequent to binding of the **chaperone** protein to **coumarin** or the **coumarin** derivative.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - **Chaperone** protein antagonist.

To demonstrate binding of a **chaperone** protein to **novobiocin**, the **novobiocin** was first immobilized on sepharose. A **chaperone** protein, either pure **Hsp90**, or a solution containing **Hsp90** in a cell lysate, was subsequently incubated with the immobilized **novobiocin**. The cell lysate was preincubated with various members of the **coumarin** family of antibiotics, namely **novobiocin**, **chlorobiocin** or **coumermycin** A1 and also ATP to determine their ability to inhibit binding of the **Hsp90**. The amount of **Hsp90** bound to the imobilized **novobiocine** was analyzed. Imobilized **novobiocin** bound in a hydrophobic manner to both of the pure **Hsp90** and the **Hsp90** present in cell lysate. Pre-incubation of the cell lysate with excess soluble **novobiocin**, **chlorobiocin**, **coumermycin** A1, or ATP inhibited, in a dose-dependent manner, subsequent **Hsp90** binding to imobilized **novobiocin**. Soluble **novobiocin** inhibited **Hsp90** binding to imobilized **novobiocin** at 8 mM. **Chlorobiocin** and **coumermycin** A1 inhibited **Hsp90** binding to imobilized **novobiocin** at 0.5 mM, while ATP inhibited **Hsp90** binding between 10 and 15 mM, as demonstrated by silver staining.

These data demonstrate that **novobiocin** binds to **chaperone** proteins such as **Hsp90** and that subsequent **Hsp90**-binding can be inhibited by contact with the **coumarin** derivatives.

USE - Used as **chaperone** protein antagonist. **Chaperone** proteins interact with a variety of proteins involved in cell proliferation. One such **chaperone** protein, **heat shock protein (Hsp)90** is expressed at 2-10 fold higher levels in tumor cells compared to their normal counterparts (see Ferrarini et al., Int. J. Cancer 51:613-619 (1992)). Method can be used to interfere with the **chaperone** protein function of **Hsp90**. The **coumarin** or a **coumarin** derivative can be used to bind **Hsp90** and to interfere with its function, including its function in tumor cell proliferation.

ADVANTAGE - Present method better suited in clinical applications compared to the use of other compounds of prior art which display in vivo toxicity unrelated to their **Hsp90** antagonism.

Dwg.0/0

TECH UPTX: 20001023

TECHNOLOGY FOCUS - PHARMACEUTICALS - The interaction between the **chaperone** protein and **coumarin** or **coumarin** derivative is such that the **chaperone** protein does not bind or binds with less affinity to its client protein or client polypeptide. Such interference with binding can be accomplished by any suitable method. Preferably the **chaperone** protein is **Hsp90** and the **coumarin** or **coumarin** derivative is **novobiocin** and the interaction is such that **novobiocin** binds a carboxy-terminal region of **Hsp90**, which contains an adenosine triphospate (ATP)-binding domain.

ABEX UPTX: 20001023

SPECIFIC COMPOUNDS - The **coumarin** or **coumarin** derivative is preferably a **coumarin** antibiotic. The **coumarin** antibiotic is **chlorobiocin** or **coumermycin** A1 or preferably **novobiocin.** The client protein or the client polypeptide is a tyrosine or serine/threonine kinase. The client protein or the client polypeptide is tyrosine kinase p185erbB2 or p60v-src, serine/threonine kinase Raf-1 or a mutated p53 protein.

L102 ANSWER 9 OF 10 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2000-364887 [31] WPIX
DNC C2000-110106
TI Dry-cleaning system for dry-cleaning of fabrics comprises dry-cleaning composition.
DC A25 A26 A97 D25 E19
IN SMITH, J A
PA (CUST-N) CUSTOM CLEANER INC; (HENK) HENKEL KGAA
CYC 83
PI WO 2000023647 A1 20000427 (200031)* EN 53 D06L001-12
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9911096 A 20000508 (200037) D06L001-12
ADT WO 2000023647 A1 WO 1998-US22243 19981022; AU 9911096 A WO 1998-US22243 19981022, AU 1999-11096 19981022
FDT AU 9911096 A Based on WO 2000023647
PRAI WO 1998-US22243 19981022
IC ICM D06L001-12
ICS C11D003-37; C11D017-04; D06L001-04
AB WO 200023647 A UPAB: 20000630
NOVELTY - A dry-cleaning system for the dry-cleaning or fabric-freshening of a fabric article comprises a dry-cleaning composition which contains polysulfonic acid and water.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (A) cleaning or freshening of a soiled fabric article (2) with (1) which comprises: (a) placing (2) and (1) into a bag which includes an opening. The opening comprises a fastening system so that the bags can enclose (2) in a vapor impermeable manner, (b) closing the system to form the bag into a closed system which comprises (2) and (1), (c) tumbling the closed system in a rotary clothes dryer at an elevated temperature, so that (1) contacts (2) to disperse the soil, and (d) opening the fastening system and removing the cleaned or freshened fabric article from the bag; (B) removing a stain from a soiled fabric article comprises steps (a), (b), (c) and (d); (C) a kit for dry cleaning or fabric freshening a fabric article comprises (1) and a bag.

USE - In dry-cleaning or fabric freshening of all fabrics, including wool, leather, nylon, cotton, polyester etc. as well as delicate fabrics such as 100% acetate, silk, rayon and blends of these fabrics.

ADVANTAGE - (1) does not include solvents like perchloroethylene or

other undesirable hydrocarbon solvents. (1) removes stains and improves the slip characteristics to fabrics (e.g. reduction in drag).
Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: A12-W12A; D11-B19; E06-A01; E06-D01; E07-A02C; E07-A03C; E10-B02A; E10-D01D; E10-E02F1; E10-E04H; E10-E04J; E10-E04L4; E10-E04L5; E10-E04M3; E10-E04M4; E10-F02; E10-G02F1; E10-G02H2; E10-H01E

AB WO 200023647 A UPAB: 20000630
NOVELTY - A dry-cleaning system for the dry-cleaning or fabric-freshening of a fabric article comprises a dry-cleaning composition which contains polysulfonic acid and water.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (A) cleaning or freshening of a soiled fabric article (2) with (1) which comprises: (a) placing (2) and (1) into a bag which includes an opening. The opening comprises a fastening system so that the bags can enclose (2) in a vapor impermeable manner, (b) closing the system to form the bag into a closed system which comprises (2) and (1), (c) tumbling the closed system in a rotary clothes dryer at an elevated temperature, so that (1) contacts (2) to disperse the soil, and (d) opening the fastening system and removing the cleaned or freshened fabric article from the bag; (B) removing a stain from a soiled fabric article comprises steps (a), (b), (c) and (d); (C) a kit for dry cleaning or fabric freshening a fabric article comprises (1) and a bag.

USE - In dry-cleaning or fabric freshening of all fabrics, including wool, leather, nylon, cotton, polyester etc. as well as delicate fabrics such as 100% acetate, silk, rayon and blends of these fabrics.

ADVANTAGE - (1) does not include solvents like perchloroethylene or other undesirable hydrocarbon solvents. (1) removes stains and improves the slip characteristics to fabrics (e.g. reduction in drag).
Dwg.0/0

TECH UPTX: 20000630
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Composition: (1) comprises (wt.%): polysulfonic acid (about 0.25 - 20) and water (about 10 - 99.75). (1) additionally comprises (wt.%): at least 1 water-miscible or partially water-miscible organic solvent (about 1 - 85), surfactants (about 0.01 - 10), gelling agents or viscosity modifiers and a compound (about 0.2 - 5) or the organic solvent is selected from glycol ethers (preferably dipropylene glycol n-propyl ether, dipropylene glycol n-butyl ether or tripropylene glycol methyl ether), 3-methoxy-3-methyl-1-butanol, liquid polyethylene glycols, 2 - 4C polyols and/or lactones (approximately g-butyro-lactone): (1) further comprises an agent selected from fabric-softening agents, anti-creasing agents, anti-soil agents, bacteriostatic agents, brightening agents, bodying agents, dyes fiber emollients, finishing agents, fragrances, germicides, lubricants, mildew-proofing agents, moth-proofing agents, shrinkage controllers and/or sizing agents. The compound which has vapor tension of at most 4 Pa at 25degreesC, is selected from 10 - 12C aliphatic alcohols, 10 - 13C aldehydes, 13 - 18C aliphatic ketones, aromatic ketones (up to 18C) having a musk odor, 8 - 15C aliphatic esters, methyl anthranilate, methyl N-methylanthranilate, p-cresyl phenylacetate, amyl salicylate, **coumarin**, **dihydrocoumarin**, gammadecalactone, dodecalactone, undecalactone, eugenol, isoeugenol, diphenyl oxide, the methyl and ethyl ethers of naphthol, galaxolide, indole and its reaction products with hydroxycitronella, tridecene-2-nitrile, and 2-(2'-methyl-pent-2'-enyl)-5-methyl pyridine. (1) is present in a spray or roll on solution, on a substrate. The substrate is selected from sheet, sponge, dauber, stick, granules or cube (preferably sheet). The bag has an interior surface, at least a portion of which has (1) releasably absorbed. The bag is formed of a flexible non-porous material which is not damaged upon exposure to agitation and to a temperature to cause the release of (1) from the surface. Preferred Method: The amount of (1) prior to step (a) is applied by rubbing, dabbing, spraying, rolling on or dipping (2)

with (1) so as to loosen and remove stain from (2).

ABEX UPTX: 20000630

EXAMPLE - The dry-cleaning composition were prepared by adding polysulfonic acid (**HSP**-1180) (i) and distilled water to a vessel with a stirrer. The solvent(s) and remaining materials such as surfactants, fragrances etc. were added individually with agitation. The system pH was adjusted after the acid is added or at the end of preparation. Two formulations of the composition were prepared. First formulation (I) comprises (%): Arcolsolv (RTM; DPNB is dipropylene glycol n-propyl ether) (ii) (42.03), Arcosolv TPM (iii) (50.95), distilled water (iv) (2.**90**), Tergitol (RTM; 15 - S - 3 is as nonionic surfactant) (v) (0.41), Igepal (RTM; CO-660 is a nonionic surfactant) (vi) (0.58), (i) (2.**90**) and Frag DC1212 (fragrance) (vii) (0.23). second formulation (II) comprises (%): Arcolsolv (RTM; DPNP is dipropylene glycol t-butyl ether) (55.96), (iii) (15.94), (iv) (25.00), (v) (0.80), (vi) (1.00), (i) (1.00) and (vii) (0.50). The formulations were tested in a stain removal procedure. Stains including spaghetti and gravy were placed on fabric, left to dry for 24 - 48 hours and gently scraped to remove the excess stain. A clean paper towel was placed under the stain on the cloth swatch. Then the cloth swatch was subjected to 10 seconds rubbing with paper towel, moved to a clean spot on the paper towel, subjected to 20 seconds further rubbing (2 times) and again moved to a clean spot on the paper. The cloth swatch was put aside to air dry. All cloth swatches were taken from fabrics supplied by Test fabrics. The fabric type for (I) was 100% worsted flannel and the stain type was Estee Lauder lipstick. The % stain removal was 100 which means no visual sign of the original stain remained on the fabric. The fabric type for (II) was span viscose challis and the stain type was Wishbone Deluxe French dressing . The % stain removal was **90**.

L102 ANSWER 10 OF 10 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2000-237778 [20] WPIX
DNC C2000-072438
TI Vaccinating mammals by administering, appropriate vector, nucleotide sequence encoding antigenic peptide and compound enhancing humoral and cellular immune responses initiated by peptide.
DC B05
IN CHARO, J; KIESSLING, R
PA (GLAX) GLAXO GROUP LTD
CYC 89
PI WO 2000012121 A1 20000309 (200020)* EN 65 A61K039-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9957402 A 20000321 (200031) A61K039-00
NO 2001000922 A 20010423 (200130) A61K000-00
EP 1107785 A1 20010620 (200135) EN A61K039-00
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
CZ 2001000717 A3 20011017 (200172) A61K039-00
BR 9913323 A 20011204 (200203) A61K039-00
KR 2001072983 A 20010731 (200209) A61K048-00
HU 2001003214 A2 20011228 (200216) A61K039-00
CN 1326358 A 20011212 (200225) A61K039-00
ZA 2001001539 A 20020424 (200237) 74 A61K000-00
AU 747643 B 20020516 (200244) A61K039-00
JP 2002523469 W 20020730 (200264) 73 A61K039-00
MX 2001002043 A1 20011101 (200279) A61K039-00
NZ 510206 A 20030829 (200365) A61K039-00
ADT WO 2000012121 A1 WO 1999-EP6217 19990825; AU 9957402 A AU 1999-57402

19990825; NO 2001000922 A WO 1999-EP6217 19990825, NO 2001-922 20010223; EP 1107785 A1 EP 1999-944505 19990825, WO 1999-EP6217 19990825; CZ 2001000717 A3 WO 1999-EP6217 19990825, CZ 2001-717 19990825; BR 9913323 A BR 1999-13323 19990825, WO 1999-EP6217 19990825; KR 2001072983 A KR 2001-702431 20010226; HU 2001003214 A2 WO 1999-EP6217 19990825, HU 2001-3214 19990825; CN 1326358 A CN 1999-812463 19990825; ZA 2001001539 A ZA 2001-1539 20010223; AU 747643 B AU 1999-57402 19990825; JP 2002523469 W WO 1999-EP6217 19990825, JP 2000-567235 19990825; MX 2001002043 A1 MX 2001-2043 20010226; NZ 510206 A NZ 1999-510206 19990825, WO 1999-EP6217 19990825

FDT AU 9957402 A Based on WO 2000012121; EP 1107785 A1 Based on WO 2000012121; CZ 2001000717 A3 Based on WO 2000012121; BR 9913323 A Based on WO 2000012121; HU 2001003214 A2 Based on WO 2000012121; AU 747643 B Previous Publ. AU 9957402, Based on WO 2000012121; JP 2002523469 W Based on WO 2000012121; NZ 510206 A Based on WO 2000012121

PRAI GB 1998-18627 19980826

IC ICM A61K000-00; A61K039-00; A61K048-00
ICS A61K039-39; A61P031-00; A61P031-12; A61P037-00; A61P037-04

AB WO 200012121 A UPAB: 20021105

NOVELTY - A method of vaccinating mammals against disease states by administering to the mammal, with an appropriate vector, a nucleotide sequence encoding an antigenic peptide associated with the disease state and additionally administering a compound that enhances both humoral and cellular immune responses initiated by the antigenic peptide.

DETAILED DESCRIPTION - The compound is 4-(2-formyl-3-hydroxyphenoxymethyl)benzoic acid, 5-(2-formyl-3-hydroxyphenoxy)pentanamide, N,N-diethyl-5-(2-formyl-3-hydroxyphenoxy)pentanamide, N-isopropyl-5-(2-formyl-3-hydroxyphenoxy)pentanamide, ethyl 5-(2-formyl-3-hydroxyphenoxy)pentanoate, 5-(2-formyl-3-hydroxyphenoxy)pentanonitrile, (plus or minus)-5-(2-formyl-3-hydroxyphenoxy)-2- dimethylpentanoic acid, 5-(2-formyl-3-hydroxyphenoxy)-2,2-dimethylpentanoic acid, methyl 3-(2-formyl-3-hydroxyphenoxy)methylbenzoate, 3-(2-formyl-3-hydroxyphenoxy)methylbenzoic acid, benzyl 5-(2-formyl-3-hydroxyphenoxy)pentanoate, 5-(4-(2-formyl-3-hydroxyphenoxy)-N-butyl)tetrazole, 7-(2-formyl-3-hydroxyphenoxy)heptanoic acid, 5-(2-formyl-3-hydroxyphenoxy-4-n-propoxyphenoxy)pentanoic acid, 5-(4,6-dichloro-2-formyl-3-hydroxyphenoxy)pentanoic acid, 5-(2-formyl-3-hydroxyphenoxy)-N-methylsulfonylpentanamide, ethyl 4-(2-formyl-3-hydroxyphenoxymethyl)benzoate, 5-(4-chloro-2-formyl-3-hydroxyphenoxy)pentanoic acid, 5-(3-acetylamino-2-formylphenoxy)pentanoic acid, aminoguanidine, 4-(2-formyl-3-hydroxyphenoxy)butanoic acid, 6-(2-formyl-3-hydroxyphenoxy)hexanoic acid, ethyl 4-(3-acetylamino-2-formylphenoxymethyl)benzoate, 4-(3-acetylamino-2-formylphenoxymethyl)benzoic acid, 2-(2-formyl-3-hydroxyphenoxymethyl)benzoic acid, 5-(4-(2-formyl-3-hydroxyphenoxymethyl)phenyl)tetrazole, 5-(2-formyl-3-hydroxy-4-methoxyphenoxy)pentanoic acid, 3-(2-formyl-3-hydroxyphenoxy)propionitrile, 4-hydroxyphenylacetaldehyde, 1-hydroxy-2-phenylpropane, 3-phenylproponionaldehyde, 4-nitrobenzaldehyde, methyl 4-formylbenzoate, 4-chlorobenzaldehyde, 4-methyloxybenzaldehyde, 4-methylbenzaldehyde, 8,10-dioxoundecanoic acid, 4,6-dioxoheptanoic acid, pentanedione, 5-methoxy-1-tetralone, 6-methoxy-1-tetralone, 7-methoxy-1-tetralone, 2-tetralone, 3-hydroxy-1-(4-methoxyphenyl)-3-methyl-2-butanone, 2',4'-dihydroxy-2-(4-methoxyphenyl)acetophenone, 2-hydroxy-1-(4-methoxyphenyl)-pent-2-en-4-one, naringenin 4',5,6-trihydroxyflavonone, 4'-methoxy-2-(4-methoxyphenyl)acetophenone, 6,7-**dihydroxycoumarin**, 7-methoxy-2-tetralone, 6,7-dimethoxy-2-tetralone, 6-hydroxy-4-**methylcoumarin**, homogentisic acid gamma lactone, 6-hydroxy-1,2-naphthoquinone or 8-methoxy-2-tetralone and their physiologically acceptable salts.

ACTIVITY - Immunostimulant; antiviral; antibacterial; antiparasitic; anticancer; antiallergic; immunomodulatory.

MECHANISM OF ACTION - None given.

USE - The methods are used to vaccinate mammals against disease states (claimed). They are used to protect mammals against a variety of disease states such as viral, bacterial or parasitic infections caused by hepatitis viruses A, B, C, D and E, HIV, herpes viruses 1, 2, 6 and 7, cytomegalovirus, varicella zoster, papilloma virus, Epstein-Barr virus, influenza viruses, para-influenza viruses, adenoviruses, coxsackie viruses, picornaviruses, rotaviruses, respiratory syncytial viruses, pox viruses, rhinoviruses, rubella virus, papovirus, mumps virus, measles virus, mycobacteria causing tuberculosis and leprosy, pneumococci, aerobic Gram-negative bacilli, mycoplasma, staphylococci, streptococci, salmonellae, chlamydiae and including malaria, leishmaniasis, trypanosomiasis, toxoplasmosis, schistosomiasis and filariasis, cancers such as breast, colon, rectal, head and neck, renal, laryngeal, ovarian, cervical and prostate cancers, and malignant melanomas, allergies such as rhinitis due to house dust mite, pollen or other environmental allergens, and autoimmune diseases including systemic lupus erythematosus.

ADVANTAGE - The method shows the dual action of stimulating humoral immune response while simultaneously stimulating the cellular immune response mechanism, to raise both serum antibody levels and cytokine T lymphocyte levels. Immunization with a plasmid DNA coding for mycobacterial **heat shock protein** (M.hsp65)
antigen was compared between for control plasmid (p3), p3 plus tucaresol (1 mg), p3M.65, p3M.65 plus tucaresol, plasmid expressing granulocyte-macrophage colony-stimulating factor (p3M.65 G) and plasmid expressing gamma interferon (p3M.65I). Significant amounts of antibodies to M.hsp65 could be detected in sera from p3M.65-immunized mice, but not in p3 immunized mice. Antibody titers were increased markedly when tucaresol was administered subcutaneously simultaneously with the M.hsp plasmid (p3M.65, T). In contrast, no increase in specific antibody response was detected in mice immunized with control plasmid and tucaresol excluding the possibility that a general increase in non-specific cross-reactive antibodies due to the high degree of immuno-potentiation associated with tucaresol administration accounted for the observed effect.

DESCRIPTION OF DRAWING(S) - Effects of tucaresol on the specific antibody response to mycobacterial hsp65 after immunization with pDNA expressing M.hsp65.

Dwg.3A/9

FS CPI

FA AB; GI; DCN

MC CPI: B04-E02F; B04-E03F; B06-A01; B07-A02A; B07-A03; B07-D07; B07-D13; B10-B02; B10-C03; B10-C04; B10-D01; B10-E02; B10-F02; B10-G02; B14-A01; B14-A02; B14-B02; B14-G01; B14-G02A; B14-G03; B14-H01; B14-S11

AB WO 200012121 A UPAB: 20021105

NOVELTY - A method of vaccinating mammals against disease states by administering to the mammal, with an appropriate vector, a nucleotide sequence encoding an antigenic peptide associated with the disease state and additionally administering a compound that enhances both humoral and cellular immune responses initiated by the antigenic peptide.

DETAILED DESCRIPTION - The compound is 4-(2-formyl-3-hydroxyphenoxymethyl)benzoic acid, 5-(2-formyl-3-hydroxyphenoxy)pentanamide, N,N-diethyl-5-(2-formyl-3-hydroxyphenoxy)pentanamide, N-isopropyl-5-(2-formyl-3-hydroxyphenoxy)pentanamide, ethyl 5-(2-formyl-3-hydroxyphenoxy)pentanoate, 5-(2-formyl-3-hydroxyphenoxy)pentanonitrile, (plus or minus)-5-(2-formyl-3-hydroxyphenoxy)-2- dimethylpentanoic acid, 5-(2-formyl-3-hydroxyphenoxy)-2,2-dimethylpentanoic acid, methyl 3-(2-formyl-3-hydroxyphenoxy)methylbenzoate, 3-(2-formyl-3-hydroxyphenoxy)methylbenzoic acid, benzyl 5-(2-formyl-3-hydroxyphenoxy)pentanoate, 5-(4-(2-formyl-3-hydroxyphenoxy)-N-butyl)tetrazole, 7-(2-formyl-3-hydroxyphenoxy)heptanoic acid,

5-(2-formyl-3-hydroxyphenoxy-4-n-propoxyphenoxy)pentanoic acid, 5-(4,6-dichloro-2-formyl-3-hydroxyphenoxy)pentanoic acid, 5-(2-formyl-3-hydroxyphenoxy)-N-methylsulfonylpentanamide, ethyl 4-(2-formyl-3-hydroxyphenoxymethyl)benzoate, 5-(4-chloro-2-formyl-3-hydroxyphenoxy)pentanoic acid, 5-(3-acetylamino-2-formylphenoxy)pentanoic acid, aminoguanidine, 4-(2-formyl-3-hydroxyphenoxy)butanoic acid, 6-(2-formyl-3-hydroxyphenoxy)hexanoic acid, ethyl 4-(3-acetylamino-2-formylphenoxymethyl)benzoate, 4-(3-acetylamino-2-formylphenoxymethyl)benzoic acid, 2-(2-formyl-3-hydroxyphenoxymethyl)benzoic acid, 5-(4-(2-formyl-3-hydroxyphenoxymethyl)phenyl)tetrazole, 5-(2-formyl-3-hydroxy-4-methoxyphenoxy)pentanoic acid, 3-(2-formyl-3-hydroxyphenoxy)propionitrile, 4-hydroxyphenylacetaldehyde, 1-hydroxy-2-phenylpropane, 3-phenylproponionaldehyde, 4-nitrobenzaldehyde, methyl 4-formylbenzoate, 4-chlorobenzaldehyde, 4-methyloxybenzaldehyde, 4-methylbenzaldehyde, 8,10-dioxoundecanoic acid, 4,6-dioxoheptanoic acid, pentanedione, 5-methoxy-1-tetralone, 6-methoxy-1-tetralone, 7-methoxy-1-tetralone, 2-tetralone, 3-hydroxy-1-(4-methoxyphenyl)-3-methyl-2-butanone, 2',4'-dihydroxy-2-(4-methoxyphenyl)acetophenone, 2-hydroxy-1-(4-methoxyphenyl)-pent-2-en-4-one, naringenin 4',5,6-trihydroxyflavonone, 4'-methoxy-2-(4-methoxyphenyl)acetophenone, 6,7-**dihydroxycoumarin**, 7-methoxy-2-tetralone, 6,7-dimethoxy-2-tetralone, 6-hydroxy-4-**methylcoumarin**, homogentisic acid gamma lactone, 6-hydroxy-1,2-naphthoquinone or 8-methoxy-2-tetralone and their physiologically acceptable salts.

ACTIVITY - Immunostimulant; antiviral; antibacterial; antiparasitic; anticancer; antiallergic; immunomodulatory.

MECHANISM OF ACTION - None given.

USE - The methods are used to vaccinate mammals against disease states (claimed). They are used to protect mammals against a variety of disease states such as viral, bacterial or parasitic infections caused by hepatitis viruses A, B, C, D and E, HIV, herpes viruses 1, 2, 6 and 7, cytomegalovirus, varicella zoster, papilloma virus, Epstein-Barr virus, influenza viruses, para-influenza viruses, adenoviruses, coxsackie viruses, picornaviruses, rotaviruses, respiratory syncytial viruses, pox viruses, rhinoviruses, rubella virus, papovirus, mumps virus, measles virus, mycobacteria causing tuberculosis and leprosy, pneumococci, aerobic Gram-negative bacilli, mycoplasma, staphylococci, streptococci, salmonellae, chlamydiae and including malaria, leishmaniasis, trypanosomiasis, toxoplasmosis, schistosomiasis and filariasis, cancers such as breast, colon, rectal, head and neck, renal, laryngeal, ovarian, cervical and prostate cancers, and malignant melanomas, allergies such as rhinitis due to house dust mite, pollen or other environmental allergens, and autoimmune diseases including systemic lupus erythematosus.

ADVANTAGE - The method shows the dual action of stimulating humoral immune response while simultaneously stimulating the cellular immune response mechanism, to raise both serum antibody levels and cytokine T lymphocyte levels. Immunization with a plasmid DNA coding for mycobacterial **heat shock protein** (M.hsp65) antigen was compared between for control plasmid (p3), p3 plus tucaresol (1 mg), p3M.65, p3M.65 plus tucaresol, plasmid expressing granulocyte-macrophage colony-stimulating factor (p3M.65 G) and plasmid expressing gamma interferon (p3M.65I). Significant amounts of antibodies to M.hsp65 could be detected in sera from p3M.65-immunized mice, but not in p3 immunized mice. Antibody titers were increased markedly when tucaresol was administered subcutaneously simultaneously with the M.hsp plasmid (p3M.65, T). In contrast, no increase in specific antibody response was detected in mice immunized with control plasmid and tucaresol excluding the possibility that a general increase in non-specific cross-reactive antibodies due to the high degree of immuno-potentiation associated with tucaresol administration accounted for the observed effect.

DESCRIPTION OF DRAWING(S) - Effects of tucaresol on the specific

antibody response to mycobacterial hsp65 after immunization with pDNA expressing M.hsp65.
Dwg.3A/9

TECH UPTX: 20000426
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method - Administration of the compound takes place on 1-7 occasions, between 14 (7; 24) days prior to and 14 (7; 24) days after administration of the nucleotide sequence. Administration of the compound is substantially simultaneous with administration of the nucleotide sequence. Administration is repeated 1-4 times at intervals of 1 day-18 months and is oral, nasal, pulmonary, intramuscular, subcutaneous, intradermal or topical, preferably by a gene-gun delivery technique. The compound is administered at a dose of 0.1-100 mg/kg/administration. The mammal is human.
Preferred Compound - The compound is 4-(2-formyl-3-hydroxyphenoxymethyl)benzoic acid.

ABEX UPTX: 20000426
ADMINISTRATION - Administration of the compound takes place on 1-7 occasions, between 14 (7; 24) days prior to and 14 (7; 24) days after administration of the nucleotide sequence (claimed). Administration of the compound is substantially simultaneous with administration of the nucleotide sequence (claimed). Administration is repeated 1-4 times at intervals of 1 day-18 months (claimed). Administration is oral, nasal, pulmonary, intramuscular, subcutaneous, intradermal or topical, preferably by a gene-gun delivery technique (claimed). The compound is administered at a dose of 0.1-100 mg/kg/administration (claimed) preferably 0.1-10 (1-5) mg/kg/administration. The mammals are human (claimed) as well as domestic animals, laboratory animals, farm animals and captive wild animals. Administration is separate, sequential or concomitant (claimed).

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